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Hans Nachtsheim

DYNAMICS OF HUMAN POPULATIONS
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Stanley M. Gartler

American Eugenics Society, Inc.

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Vol. 2, No. 1, March 1955

Eugenics Quarterly

EDITORIAL COMMENT

The Prospect for Eugenics

Annual Report, 1954
American Eugenics Society, Inc.

The year 1954 may well mark the beginning of a world-wide interest in the quality of populations.

The World Population Conference was held in Rome in September 1954. One of its sections considered the effect of population change on the distribution of genetic factors. This section discussed the prevalence of genetically based deficiencies, the detection of carriers of recessive genes, factors affecting mutation trends in the distribution of genes, the role of twin studies, the need for research in population genetics. Over thirty papers were prepared for this section, and these were discussed by representatives of more than forty nations, including several from behind the Iron Curtain. Only the representatives of the Soviet group dissented from the view that there was a genetic basis involved in the development of population quality. At the International Genetic Symposium held in Italy on September 7, 1953, the Pope himself made this significant statement:

> "The deterioration of hereditary factors must be prevented. As far as possible, deficiencies already in evidence must be remedied and care must be taken that hereditary factors even of little value be not allowed to deteriorate still further by fusing them with a homozygote partner. On the other hand, it must be seen to that positive characteristics at their full value join with those whose hereditary patrimony is similar."[1]

It has never been more important for the eugenics movement to handle itself with wisdom, restraint, and clarity of purpose. To this end the American Eugenics Society has continued to build its membership only from among those who combine respect for the integrity of scientific findings with an earnest desire to raise the average genetic potential of future generations. By being ready to alter its course in the face of new findings, by its determination to go no further than the scientific findings allow, by avoiding easy popularization, fanatical measures, or the enunciation of absolutes—in these ways the Society has endeavored to encourage and even to direct the present growth in eugenic thinking.

The position of eugenics at the close of 1954 may be briefly summarized. Medical genetics has seen great advances in the past fifteen years, and these are finding expression in increased recognition by the medical profession, more research, greater use of heredity clinics, and—in the Scandinavian countries at least—advances in the national registration of hereditary defectives. Population genetics has recently moved from the theoretical to the practical with the work done on the distribution of the blood groups among different peoples and in different areas. Anthropologists are working on entirely new clues for the differentation of group qualities. Only the field of individual and group differences in intelligence and personality seems to have made little

[1]Eugenical News, Vol. XXXVIII, No. 4, p. 147.

advance. There are a few instances of reversals in social-class differentials in births, but there is no apparent increase of knowledge bearing on the genetic advantage or disadvantage for future generations of having a larger proportion of the children born to the more responsible parents. Research is greatly needed in this field. But it is hard to believe that such a trend in births would bring about genetic deterioration.

Meetings

The 1954 Annual Meeting was held at the Hotel New Yorker in New York City on December 17 in conjunction with a conference of the American Social Hygiene Association. Frederick Osborn, Secretary of the Society, spoke at the luncheon on the topic, "Involving the Whole Community in Education for Personal and Family Living."

The 1955 Annual Meeting will take place at Philadelphia on April 22 in cooperation with the Groves Conference on Marriage and the Family. The Society will participate in a morning research session and afternoon general session, after which the business meeting is scheduled.

A workshop will be conducted in New York City on May 5, 1955 in connection with the Annual Meeting of the Planned Parenthood Federation of America.

Publications

EUGENICS QUARTERLY, the new journal of the Society, was launched in March 1954. The Quarterly has printed original articles in genetics, population, family life, and eugenics by outstanding scientists both in this country and abroad. European scientists have displayed a great deal of interest in the new journal and played a real part in giving it substantial content. The Quarterly has thus reflected the international point of view, as well as interpreting the eugenics movement in this country. There is no other periodical in the United States devoted solely to the qualitative and genetic aspects of populations and of individual growth or concerned with the development of a practical philosophy and program of eugenics.

The paid circulation of the Quarterly is now more than double that of its predecessor, *Eugenical News*.

Reprints and Pamphlets: Nearly 18,000 copies were distributed during the year. Since September the Society has been obliged to charge twenty-five cents a copy, for the number of requests made the cost of free distribution too great. The pamphlet most in demand has been "Preparing for Parenthood," of which nearly 3,000 copies were distributed during 1954. This publication has been listed for use by such groups as The American Red Cross, the YMCA, the Maternity Center Association, and family groups in Puerto Rico. Parents from every section of the United States have written in for it.

The Society and its publications have been written up in the following newspapers and periodicals: *The New York Times, The New York Herald-Tribune, The Washington Post-Herald, Science Newsletter, Science, AIBS Bulletin, Marriage and Family Living, American Sociological Review, Mental Hygiene, Population, Journal de Génetique Humaine, Eugenics Review, Bulletin of Current Literature, Bulletin of International Conference of Social Workers, Family Life, Newsletter of the Association for Family Living, News of Population and Birth Control, Family Life Bulletin, Briefs, Sight-saving Review.*

Research

Twin Study: A grant of $2000.00 was made in 1952 to the American Eugenics Society for the development of proposals for a major, long-term study on twins. Plans for such a study were discussed at a meeting of the Board of Directors, and the officers were authorized to make further contacts. During 1953 the Population

Council expressed its interest by a grant of $5000.00 for the same purpose, and the National Research Council and the Social Science Research Council prepared to appoint a joint committee to consider the planning of such a study.

In the spring of 1954 a meeting was held in the offices of the Social Science Research Council of a group which included the following: Alfred Baldwin of Cornell, Milton Senn of Yale, Don Marquis of the University of Michigan, Harry L. Shapiro of the American Museum of Natural History, Pendleton Herring and Brewster Smith of the Social Science Research Council, and Frederick Osborn. At this meeting, Dr. Shapiro and Mr. Osborn were asked to report on the number of twins born in New York City each year, according to type of twin and by hospital, and the number of twins placed out by adoption agencies. This survey was made by Lester Firschein and was completed on November 1, 1954. It is now in the hands of Marquis, Shapiro, and Osborn, who are considering the next steps to be taken.

Medical Handbook: The drafting is almost completed on Dr. C. Nash Herndon's handbook for general practitioners, which is sponsored by the New York Academy of Medicine and financed by the American Eugenics Society. The book should be ready for publication some time in 1955.

Membership

The concentrated effort made to secure new members during 1954 resulted in more than doubling the membership. The drive will be continued in 1955. As in the past, only those persons will be accepted for membership who either have a scientific background or an established willingness to accept scientific findings as the basis of eugenic advance. A special membership fee of $2.50 (regular membership, $5.00) is being offered outside the United States and Canada to take advantage of the wide interest shown in EUGENICS QUARTERLY overseas.

The Society urgently needs a broader financial base. The grant made by the Pioneer Fund in 1952 runs out in June 1955 and must be replaced. The major support of the Society has come in recent years from the interested scientific disciplines. The Society now needs to strengthen its group of lay members, for the better handling of its administrative affairs and to begin enlarging public understanding of eugenics problems.

The time is not yet ripe for the full public acceptance of the eugenics ideal. But there have been indications during 1954 that such a time may be approaching. During 1955 the Society will make every effort through the stimulation of research, through publications, and through scientific discussion to hasten this change.

FREDERICK OSBORN
Secretary
December 31, 1954

To The Editor:

The article by Gardner Murphy, presented as an editorial in EUGENICS QUARTERLY, December 1954, gives a powerful stimulus toward imaginative thinking about the requirements for real progress in eugenics, both as regards research needs and as regards present policies in social action.

As Murphy points out, there is at present no well-formulated conception of research needs with respect to the distribution and transmission of genetic factors affecting the most important intellect-personality characteristics, apart from research on certain isolated, disturbing traits.

One suggestion that might be drawn from this analyisis is that provision should be made for systematic exploration of this problem on the conceptual level, leading toward the design of possible research approaches. Some scientist who comprehends the problem might be enlisted to spend a considerable time in an attempt to provide such a formulation—in conference with specialists in various fields, including brain physiology, the ecology of mental disease, human genetics, etc.—if proper sponsorship and financial support could be obtained in this way some possible lines of fruitful research that are already apparent could be developed more systematically, and other leads might be discovered.

One important approach in this field may be found in new studies on the physiology of intelligence and personality. Genetic factors can only affect intelligence and personality *through* effects on brain structure, vascular structure, gland structure, and other physical conditions of chemical, electrical, and other physiological processes. We assume that there is no "mystic" link between constitutional factors in successive generations; various physiological processes are the necessary links between genes and personality. The paucity of our knowledge about these physiological links seems to me to be the major bottleneck that is blocking progress in this field. Real progress has has been made on the physiology of epilepsy, but little progress has been made on the physiology of schizophrenia or various kinds of intellectual genius. Perhaps the most promising advance along this line during the last few decades came through the discovery of genetic factors affecting the question of phenylpyruvic acid and its functional significance and through studies of the Rh factor and other blood factors.

An entirely different approach of great theoretical importance for eugenics lies in studies on relations between (phenotypic) personality characteristics and fertility. Such studies are important from the standpoint of social policy; they also have theoretical importance in studies on the qualitative significance of differential fertility.

There has, in my opinion, been rather serious neglect both in demographic research and in the program of the American Eugenics Society of factors responsible for the persistently high fertility of some depressed, problematic classes even within urban communities where there is widespread knowledge about anti-natal measures. There has been more interest in the program of the American Eugenics Society in conditions affecting the size of family of gifted individuals, but there has been no serious research on this subject.

As regards practical programs at present, there is a great gap between "eugenics" and "euthenics." It is commonly assumed that, in theory, eugenics is concerned only with the *genetic* aspects of the distribution of the births. Euthenics is concerned with the *nurture* of children but not with the distribution of births. Eugenics denotes the field of child study associations, family life associations, and many social welfare programs. The eugenics movement, under Osborn's inspiration, now concerns itself with the social characteristics of parents *in so far as* these are assumed to be associated with genetic factors having similar tendencies. It thus sets up "The Eugenic Hypothesis" as a condition of its interest in the distribution of births in relation to characteristics of parents. There is *no* organized interest, free from any doctrinal assumptions on the nature-nurture question, in the qualitative aspects of population trends.

It would be entirely rational, from a social standpoint, to promote an increase of parenthood in families with superior education and interest in child life and a decrease of parenthood among those with the opposite characteristics among persons with the same genetic characteristics. An assumption of positive association between phenotypic and genotypic characteristics provides an added motivation among persons with interest in genetics, but insistence on this position in the absence of conclusive scientific evidence alienates some scrupulous scientists and many persons with deep attachment to equalitarian sentiments. From an operational standpoint, the distinction between genetic and environmental factors is important only where they have divergent implications for policy—as, for example, in the case of fine people who are concerned about the possible transmission of some genetic defect.

I therefore recommend that the eugenics movement extend its interest to the whole field of the qualitative aspects of human reproduction. This would be consistent with continued emphasis on research on the genetic aspects of this problem—and one of the major functions of the Society would be to plan and promote such significant research, which otherwise tends to be neglected by scientists in the relevant specialized disciplines. But the society might also concern itself with promoting a healthy distribution of births as regards the *actual characteristics* of potential parents, regardless of any assumption about the roles of hereditary and environmental factors in the determination of these characteristics, *except* where there is specific scientific evidence on genetic factors. I can see no reason against an enlarged conception of "eugenics" to include both the genetic and environmental aspects of "good birth," except perhaps a sense of loyalty to Galton and other previous exponents of a tradition formed at a time when social and psychological sciences were less advanced.

The minimal "Eugenic Hypothesis" required for such an enlarged program is that, in the absence of scientific evidence with respect to the genetic basis of particular conditions, it is assumed that there is no *negative* correlation between socially desirable genetic characteristics and observed parental characteristics in children. The new eugenics movement could then include interests in all aspects of the familial background of children to be born —thus extending its interest to fill the gap noted above between eugenics, as previously defined, and euthenics.

This line of thinking might lead to some attempt to sponsor a journal on all qualitative aspects of population trends—and this might have an international character. But I see no adequate support for such a venture, and it would necessarily have rather limited appeal. EUGENICS QUARTERLY, in spite of its assumed primary orientation toward genetic issues and doctrinal implications, already has very much this character.

Another possibility might be an attempt to seek enlarged social appeal in association with other organized movements concerned with the family and child welfare. But, as already noted, no social movement is oriented toward primary interest in the distribution of births in relation to the characteristics of parents.

I will be interested in any responses by the Editor or by other members of the Society to these suggestions.

FRANK LORIMER
The American University

ANNUAL MEETING 1955

American Eugenics Society, Inc.
230 Park Ave., New York 17, N. Y.

To be held in Philadelphia, Pa. on April 22, 1955 in conjunction with the Groves Conference on Marriage and the Family.

RESEARCH SECTION (Morning)

"Influence of Heredity on Famly Health"

Speaker—Dr. Barton Childs, Pediatrician at the Harriet Lane Clinic, Johns Hopkins University

Chairman—Frederick Osborn, Secretary, American Eugenics Society

Discussants—Gordon Allen, M.D. Research Division, National Institute of Mental Health; Stanley Gartler, Institute of Human Variation, Columbia University

GENERAL SESSION (Afternoon)

Panel Discussion

Speakers — Frederick Osborn, "The Make-up of the Healthy Family; C. Nash Herndon, M.D., Department of Medical Genetics, Bowman Gray School of Medicine, "Heredity Counseling"

Chairman—Franz J. Kallmann, M.D., N. Y. State Psychiatric Institute

Discussants—Robert C. Cook, Director, Population Reference Bureau
General Charles A. Lindbergh
Frank Lorimer, Professor of Population, The American University
Emily Mudd, Director, Philadelphia Marriage Council

BUSINESS MEETING (After General Session)

Open to all members of the American Eugenics Society

In Memoriam

Maurice A. Bigelow

Maurice A. Bigelow passed away at the age of eighty-two on January 6, 1955, in Peekskill, N. Y. Dr. Bigelow was Honorary Secretary of the American Eugenics Society and a Director at the time of his death. He had been President, Secretary, and Managing Editor of the Society at various times in the last two decades. The American eugenics movement owes him an unpayable debt for his devotion to the cause of eugenics in the years when organization was lacking. The following tribute was written by Dr. Paul Popenoe, a long-time associate of Dr. Bigelow and a pioneer himself in eugenics, who gave Dr. Bigelow faithful cooperation through the years in his successful efforts to keep the Society alive.

The death of Maurice A. Bigelow takes one of the last pre-Mendelian students of heredity and one of the last generalists in the field. Specialists are now in control, and few college graduates today ever get the firm grasp of the broad principles of evolution that was given a half century or more ago by such teachers as David Starr Jordan, and that Dr. Bigelow himself always tried to give. With the increasing amount to be learned, it is becoming almost impossible for anyone to be a generalist; yet that point of view is needed more than ever. Perhaps undergraduate courses might at least be expected to provide this foundation, though few of them do so.

In his early life, Dr. Bigelow worked on such subjects as the development of Crustacea and he always had the greatest respect for research, but his life work was largely the development of methods of teaching rather than research. Here again his influence will be missed. He had nothing but contempt for those whose teaching was not tied to first-hand experience in the field or laboratory, and I well remember his indignation when he learned that one teacher's college was giving a Ph.D. in biology to pedagogues whose training included not a single hour in the laboratory.

He was a good field naturalist, and much of his activity during the first decade of this century was devoted to promoting that subject. He founded (1905) and edited the *Nature Study Review* and wrote several books in collaboration with his wife. But his wide interests and practical concern with human betterment quickly led him to concentrate on the application of biological knowledge to immediate human problems. His pioneer work in sex education was so sound that his book on that subject, first appearing in 1916, was published in the last of its revisions not many years ago and is still quoted. Public health, social hygiene, education for family life, and eugenics all commanded his support and his productive collaboration. During his forty years at Teachers College, Columbia University, as Professor of Biology and Dean of the School of Practical Arts, he was in a position to influence the education of thousands of persons. Although most of his time was taken up by administration, he insisted on teaching some courses himself, particularly human heredity, and I felt it a very genuine compliment when he entrusted this favorite of his to me during the summer of 1927 and a number of succeeding years.

Dr. Bigelow was always receptive to new ideas and eager to examine anything brought forward as a new fact, but he sub-

jected everything relentlessly to scrutiny from the biological point of view, and to the tests of logic and common sense. He was therefore not at all partisan or doctrinaire but eclectic and conservative to a degree that antagonized cultists. I think it might be said that he was somewhat prejudiced in favor of biologists, but even then he was picturesquely outspoken in his denunciation of what he considered superficiality and bluff. He was always for the genuine as against the sham, for the biological fact as against metaphysical speculation, for the logical and proved as against the hypotheses so recklessly thrown out as facts by psychoanalysts, and for observation as against mere theory. This last point is well illustrated by his little book on adolescence (1924) which topic at that time was still viewed largely in the light of extreme theories set forth by G. Stanley Hall and his followers as well as by the Freudians. "Don't take anybody's word for it," Dr. Bigelow said in effect. "Just look around and see for yourself." And he went on to show that instead of a period of sensational "storm and stress," adolescence was commonly a quiet and normal development through which boys and girls passed with little disturbance.

Many will remember him best as host at luncheons in the Faculty Club where he usually monopolized the conversation. He always enjoyed puncturing myths (particularly those that were very dignified and academically respectable) with the sharp point of an anecdote or a fact. Those who were invading his beloved field of human ecology with no more preparation than the valor of ignorance were the particular object of his barbs. After that, he liked to turn the conversation to his farm up the Hudson, to his orchard, his flowers, his dogs, and the woodchucks that were his perpetual enemies.

Dr. Bigelow was always ready to give his time and influence to any movement that he thought useful without asking for recognition or "What is there in it for me?" It was perhaps characteristic that he became President of the American Eugenics Society just before the outbreak of World War II. With everyone else being called into government service, the organization had very nearly come to an end. He was determined that it must be kept going even though others favored giving up. For six years he preserved its life almost singlehanded, and at much personal expense, with such assistance as a few others could give him from a distance. Throughout, however, he was calling attention to the need of a completely new foundation under it, a foundation made up of younger men and women who would look on it as something to which they wanted to dedicate part of their lives. He had a plan (never carried out) to circularize teachers in all the colleges in North America and ask each of them to nominate at least one graduate in the past ten years who might have the understanding and enthusiasm to help create a permanent and active organization.

His own association with the eugenics movement dated almost from its beginning. His influence was always for balance, sanity, and avoidance of extremes. His long training in college administration made him unwilling to go ahead of public acceptance. He often irritated those who pushed some point of view that he thought was not based on "Human Ecology," but even those who differed with him most strongly never questioned his honest and complete devotion to social welfare and human betterment.

PAUL POPENOE
Director
American Institute of Family Relations

FREQUENCY AND DISTRIBUTION OF PATHOLOGIC GENES IN HUMAN POPULATIONS

The Effect of Mutation Rate and Mutagenic Factors, Selective Pressure and Counter-selection*

Berlin-Dahlem
Max-Planck-Institut, f. vergl. Erbbiologie u. Erbpathologie
HANS NACHTSHEIM

THROUGH EXPERIMENTAL GENETICS, which uses plants and animals as its objects of research, we have gained a wealth of knowledge in recent decades permitting us to evaluate to a large extent the significance for the evolutionary process of the factors mentioned in the title of this paper. The situation is completely different in the case of human beings who are very awkward subjects owing to the impossibility of carrying out crossbreeding experiments with them. It is therefore not surprising that our knowledge should still be quite limited with respect to the effect of such factors of evolution as mutation and selection on the genic composition of human populations over the generations. The fact that general conformity to the laws of heredity applies to human beings no less than to plants and animals and that it has therefore been possible to draw important conclusions concerning human beings from the results of experimental research does not relieve the human geneticist of the task of collecting data on human beings and of attacking the problems with distinct methods enabling us to evaluate the peculiarities of the course followed by the domesticative and evolutionary process of the human race. To a considerable degree, this task is yet to be undertaken. In presuming to speak here of the rate of mutation and mutagenic factors, selective pressure and counterselection in their effort on the frequency and distribution of pathologic genes in human populations, I can hardly report any positive results, nor do I wish to rely on the results of experimental research to speculate on what might be the case with respect to human beings; I should rather—to the extent that this is possible within the present frame of reference—like to present in the following remarks an outline of the problems involved and tasks confronting future research.

*Given at the World Population Conference, Rome, September 1954.

The Rate of Mutation

As in the case of plants and animals, in man too the tendency toward mutation, *i.e.*, the mutation pressure, also varies with the individual genes. At least one mutation of a gene, *i.e.*, the development of two distinct forms of a gene, two alleles, is in fact the very prerequisite for the concept of the gene as such. To cite an example: the mutative change in the holandric gene which leads to Ichthyosis hystrix gravior, *i.e.*, to the development of the so-called porcupine man, has been observed or recorded in the literature only once. The first bearer of this character appeared in England in 1717. He transmitted it to all his male descendants: his 6 sons, several grandsons, great-grandsons, etc. The character lasted for 6 generations but then died out in the 19th century, and with it the changed allele. The skin changes in these definitely vital porcupine men are so striking that one might indeed have expected a report on the subject if a second mutation of the gene had been observed in some civilized country during the

last centuries.

Still other examples of single mutations of human genes could be cited and, via hereditary diseases which have occurred by way of mutation only twice or independently of one another on but a few separate occasions, we have arrived by continuous succession at diseases which can be characterized as "ever sporting diseases" (Goodman and Reed) as a result of the strong tendency toward mutation on the part of the correlated genes. However, in the case of most hereditary diseases we unfortunately still lack an adequate picture of their frequency and distribution throughout the various countries and continents, and among the various races, *i.e.*, a picture which is necessary in order to be able to classify every hereditary disease in a specific category with respect to the mutability of its gene. Here, too, but one example.

Huntington's chorea, a serious nervous disorder not too infrequent in European countries, reflects a simple dominant course of autosomal transmission, generally of 100 per cent penetrance, although as a rule this does not occur until an advanced age. The onset of the disease occurs between the ages of 30 and 40, but often even later, *i.e.*, at a period when the patients have already reproduced. In spite of the seriousness of the disease, the selective pressure is therefore slight and the disease often asserts itself very stubbornly throughout several generations in the individual family strains. For instance, in the United States it has been possible to trace the big choreatic family strains back to the 17th century. Previously, the disease is not presumed to have existed in North America and, according to the reports, 962 cases of Huntington's chorea in the U.S. are all believed to go back to 6 or 7 ancestors (probably including 3 brothers) who emigrated from England in the 17th century (Davenport).

In Europe, too, it is often possible to trace the disease back for several family generations. There is also a tendency to assume that Huntington's chorea, at least in Europe, is subject to repeated renewal as a result of frequent new mutations of the correlated gene (Kemp). Such new mutations can be regarded as applicable to those cases where both parents of a chorea patient are normal, if these parents have reached an advanced age. Julia Bell has the distinction of having assembled all of the relationship tables of patients afflicted with Huntington's chorea published up to 1934. These include 151 genealogical tables, some of them extending over 5, 6 and 7 generations, and covering 991 chorea cases (511 males, 445 females, 35 sex unknown). They include 6 family strains whose oldest choreic in the genealogical series is descended from two completely healthy parents who died at an advanced age. Should these 6 cases be regarded as new mutations? Involved are 5 European family strains and a North American one; the only thing recorded concerning the latter is that the proband was born in Brooklyn and that his father also suffered from chorea, although the parents of the latter died at the ages of 93 and 87, respectively, without any sign of choreatic disease; there is no information in the report (Smith) as to where the proband's parents and grandparents had lived.

At any rate, the material available thus far is too scanty to permit comparative evaluation of the frequency of the disease in the Old and New Worlds, or even the assumption of a different frequency of mutation in both areas. It is noteworthy that not one authentic case of Huntington's chorea has yet been reported from Japan (Komai).

Given the relatively simple and clear-cut hereditary conditions as well as the well-known clinical picture of Huntington's chorea, a general survey of the incidence of the disease in the civilized countries should present no insuperable difficulties. With international cooperation, it should thereby be possible to compile data which would enable us to answer many of the questions with respect to the genogeography and population genetics of the disease which we

have only briefly touched upon here.

But let us consider the hereditary diseases for which previous attempts have been made to calculate the rate of mutation. These diseases are approximately 20 in number. We are omitting those characterized by recessive transmission because from the very outset there is too great a factor of uncertainty to permit reliable evaluations. Most suitable for calculation are simple dominant hereditary diseases with 100 per cent penetrance as well as those characterized by sex-linked recessive transmission. The following survey includes the 7 autosomal dominant and the 2 sex-linked recessive diseases, with indication of the calculated rates of mutation. In the case of certain diseases, two calculations have already been carried out in various countries (a and b in Table 1:) this applies to chondrodystrophy in Denmark and Sweden, to retinoblastoma in London and Michigan (U.S.), to hemophilia in London and Denmark and to progressive muscular dystrophy (pelvic girdle form) in Utah (U.S.) and Northern Ireland.

TABLE 1

Disease		*Rate of mutation*
Epiloia (tuberous sclerosis)		$4\text{-}8 \times 10^{-6}$
Chondrodystrophy	a.	$4.2\text{-}4.8 \times 10^{-5}$
	b.	7×10^{-5}
Pelger's nuclear anomaly		2.7×10^{-5}
Aniridia		1.2×10^{-5}
Retinoblastoma (glioma retinae)	a.	1.4×10^{-5}
	b.	2.3×10^{-5}
Thalassemia		4×10^{-4}
Sickle cell anemia		1×10^{-2}
Hemophilia	a.	2×10^{-5}
	b.	3.2×10^{-5}
Progressive muscular dystrophy	a.	1×10^{-4}
	b.	$4.54\text{-}6.47 \times 10^{-5}$

There are two basic methods for calculating the rate of mutation, a direct and an indirect one. The direct method is very simple, but its applicability is limited. It follows the formula: Rate of Mutation

$$u = \frac{\text{Number of New Mutants}}{2 \times \text{Total number of Individuals}}$$

The formulas for the indirect method differ according to the type of hereditary transmission:

Dominance	$u = \frac{1}{2}\ (1\text{-}f)\ x$
Recessiveness	$u = \quad (1\text{-}f)\ x$
Sex-linked recessiveness	$u = \frac{1}{3}\ (1\text{-}f)\ x.$

In these formulas u represents the rate of mutation; f, the relative reproductive fitness of the mutant; x, the relative frequency of the mutants in the population. (I demonstrated the use of these methods on the basis of examples cited in a communiçation in the 1954 issue of *Naturwissen-schaften.*)

In calculating the rates of mutation, careful consideration must be given to many possible sources of error. In my opinion, such care has, as a rule, not been sufficiently exercised hitherto, and I would maintain that this has resulted almost universally in the calculation of excessively high rates of mutation. On this subject, too, we can cite but a few examples.

First of all, the number of mutants for whom the rate of mutation is to be calculated must not be too small in the population under study. The calculation is worthless when, as happened in one instance, it is based on *one* case in 44,000 births of a disease which was, moreover, of the recessive hereditary type. When Pätau and I calculated the mutation rate for Pelger's nuclear anomaly in 1946, our material was likewise still very limited and at the time we explicitly attached less importance to the results than to the demonstration of the *method.* Since then, the data on Pelger's nuclear anomaly have increased substantially and it has been possible to make a new calculation on a broader basis. It is interesting to compare the results. In 1946 we reached a mutation rate (u) of approximately 1:10,000 (1×10^{-4}) for Pelger's anomaly; today, the results indicate a rate of 1:37,000 (2.7×10^{-5}).

The material on Pelger's anomaly also serves to illustrate another source of error. As already stated, cases where the carrier of

a 100 percent penetrant-dominant hereditary disease has two normal parents are in general considered new mutations. However, it is possible for an error originating with illegitimacy to creep in. Such a source of error can be eliminated through a paternity examination. In the available data on Pelger's anomaly there are 4 cases in which both parents were non-Pelger individuals. In 3 cases paternity was established positively by examination; in the fourth case it was not possible to make the examination and certain doubts actually do exist with respect to the paternity involved. Now if in calculating the rate of mutation we therefore omit the uncertain case, we obtain the result already indicated: *u* equals 1:37,000. If we are less conservative, however, and include all 4 new mutations in our calculation, we arrive at *u* equals 1:28,500. With *one* new mutation less, the estimated rate of mutation for this material drops from 3.5×10^{-5} to 2.7×10^{-5}. (Detailed information will be found in my report "Die Mutations rate menschlicher Gene" in *Naturwissenschaften,* 41, 1954, 385.)

False diagnoses can also give rise to excessively high estimates of the rate of mutation, as illustrated by the case of thalassemia, for which the very high rate of 4×10^{-4} was calculated, *i.e.,* 400 mutated alleles per one million gametes. The heterozygous carriers of the thalassemia gene show evidence of being afflicted with thalassemia *minor* which is harmless and which can only be detected in the blood picture, whereas the homozygous carriers suffer from thalassemia *major,* or Cooley's anemia, which is almost always fatal during childhood. It is obvious then that a homozygous individual with Cooley's anemia can only be the product of the union of two heterozygous parents. Now Silvestroni and Bianco have examined the parents of 31 children hospitalized with a diagnosis of Cooley's anemia and found a completely normal blood picture in the case of 5 sets of parents. The diagnosis proved to be false in these cases: the clinical picture showed an erythroblastic anemia which resembled fatal Cooley's anemia but which was actually relatively harmless. This was further demonstrated by the fact that the 5 children of the parents with a normal blood picture were cured. In the case of thalassemia and even more so of sickle cell anemia, for which the highest known rate of mutation for a human gene has been calculated (10,000 mutated alleles per 1 million gametes!), it is probable that other sources of error, which have thus far not been compeletely clarified, are involved (Allison).

One final example. We know today that in many hereditary diseases the same or at least a very similar clinical picture can be produced not only by different genes ("heterogenie") but also by non-hereditary phenocopy caused by exogenous factors. If heterogenes or phenocopies play a role in a hereditary disease, this factor represents another very serious source of error in calculating the rate of mutation.

Retinoblastoma is a highly malignment tumor of the eye in infancy, and it has been established that its transmission is simple dominant, with high (ca. 80 per cent) penetrance. Two calculations for the rate of mutation are available: one for London (1.4×10^{-5}), the other for Michigan (2.3×10^{-5}). However, in comparison with the number of sporadic cases, the number of retinoblastoma cases concentrated in families is slight. Since prior to the development of present-day operative techniques children with retinoblastoma almost always died, the possibility of transmitting the changed allele existed only if the disease failed to manifest itself, and there was an inclination to consider the sporadic cases as new mutations in the calculation of the mutation rate.

In the meantime, my collaborator F. Vogel recently investigated a third population group (Berlin-Brandenburg area) with respect to the disease and, on the basis of certain considerations, came to the conclusion that the sporadic cases of retino-

blastoma were for the most part *non*-hereditary. It can be calculated on the basis of the data that, as a result of the therapeutic successes achieved in treating retinoblastoma in recent decades (by surgery, irradiation), at least 20 per cent of all the retinoblastoma carriers belonging to the generation of parents of the present patients have reached the stage of normal reproduction. This should be reflected by an increase in the number of demonstrably hereditary cases. No such increase has taken place. Moreover, with hereditability in all the sporadic cases, up to 50 percent of the descendants of surviving retinoblastoma carriers would in turn presumably be afflicted with retinoblastoma, a percentage which is somewhat reduced only as a result of the less than 100 per cent penetrance. Unfortunately, the available data on this subject are still very inadequate. I have already called for international collaboration in this question which is also very important from the viewpoint of eugenics because only in this manner can representative family series be compiled. The available results, however scanty, are nevertheless striking: of 42 children, only *three* (*i.e.*, 7 per cent instead of 50 per cent) have the disease.

Vogel came to the conclusion that a maximum of 25 per cent of the sporadic retinoblastoma cases are new mutations. For the moment, the question as to whether the remaining 75 per cent should be considered phenocopies caused by exogenous factors or somatic mutations is left unanswered. Of course, the resultant calculation of the mutation rate gives a completely different picture. The following is a comparison between the calculations of the previous authors and those of Vogel for the three populations investigated: Where previous authors estimate 14–23 mutated genes per 1 million gametes, according to Vogel's calculation there are only 4.4 per 1 million. This would mean that the retinoblastoma gene is the most stable of all human genes for which calculations have been made to date.

TABLE 2

	Rates of Mutation	
Authors	*According to other authors*	*According to Vogel*
Philip-Sorsby	1.4×10^{-5}	5.7×10^{-6}
Falls-Neel	2.3×10^{-5}	6.0×10^{-6}
Vogel		4.3×10^{-6}
		4.4×10^{-6}

These few examples will suffice to indicate the uncertainty of the foundations on which we are presently calculating the mutation rate of human genes, even in the case of relatively simple and clear-cut (autosomal-dominant) hereditary transmission. These are merely preliminary and tentative efforts and much preparatory work remains to be done before reliable data on the frequency and distribution of pathogenic human genes are available to us for calculating the mutation rates of such genes on a fairly sound basis.

Mutagenic Factors

If our knowledge concerning the frequency of mutation of individual human genes can be considered slight, we must confess that we have practically no positive knowledge at all regarding the effect of mutagenic factors on human hereditary characteristics. Thus far, therefore, we are left with nothing but the conjecture that the factors proven to be mutagenic in the case of other organisms are likewise mutagenic in human beings.

Since Muller first reported in 1927, that, using X-rays, he had succeeded in effecting a substantial increase in the mutation rate among Drosophila, irradiation genetics has become an important field of research in experimental genetics in its own right. After Charlotte Auerbach obtained similar results in Drosophila with mustard gas during the last war, a new area of research developed alongside that of irradiation genetics, *i.e.*, chemicogenetics, which investigates the effect of chemical substances on hereditary characteristics. On the basis of

experiments carried out thus far with animals and plants, the principal mutagenic factors are the following: all short-wave rays; hard, medium and soft X-rays; radium rays (beta and gamma rays); high-speed neutrons; ultraviolet rays; extreme temperatures (temperature shocks); and, among the chemical substances, mustard gas, formaldehyde, phenol, numerous carcinogenic substances.

With respect first to the effect of irradiation on hereditary traits, the result has been that the mutagenic effect increases with the dosage. At an irradiation of 30–40 roentgen, the spontaneous rate of mutation in Drosophila doubles; at 100 roentgen, it is tripled; at 1,000 roentgen, it increases 22-fold (Muller, Timoféeff-Ressovsky). Of particular importance, however, is the finding that there is no threshold value *below* which the rays are inactive; on the contrary, there is a cumulative effect when extremely small amounts of radiation continually strike germ cells. These results of experimental irradiation genetics had an alarming effect. The question arose as to whether, under these circumstances, patients undergoing X-ray and radium therapy (and even more so, the attending physicians and assistants), as well as all persons engaged in the testing of materials in X-ray and radium plants, in the production of X-ray tubes and in the obtaining and processing of radium, are not to a greater or lesser extent exposed to the risk of germ-cell injury. If a nurse in a modern radiotherapy institute receives an average daily dose of 0.8 roentgen, this represents approximately 240 roentgen per year of 300 working days (Zimmer). At a daily dose of 0.25 roentgen and with only 200 working days per year, a medical X-ray specialist is exposed to a total dose of 750 roentgen (Jäger and Stubbe). These data show the necessity for effective protection against irradiation in all work involving short waves.

Since injury from irradiation affects the individual less than his descendants, it will be possible to provide evidence with respect to human beings only over long periods of time and through the observation of several generations. However, even in the case of the individual exposed to irradiation, such injury may manifest itself in the form of reduced fertility. The number of childless marriages among X-ray physicians and technicians (17 out of 55 = 31 per cent, according to Loeffler) is reported to be higher than among the average population. In 18 per cent of the men, damage to the semen was detected; in some cases, the lesion receded and it even became possible to procreate phenotypically normal children. An increased number of miscarriages has been reported among women who were once X-ray assistants (Naujoks), but this is not necessarily the result of injury to the germ cells. At any rate, these observations with respect to human beings are still insufficient to provide us with a picture of the real hereditary damage resulting from work with short-wave rays. Natural irradiation, *i.e.*, spontaneous cosmic radiation, high-altitude radiation etc., is so slight that its harmful effect on germ cells scarcely needs to be taken into account.

As mentioned above, it is only in the last fifteen years or so that chemical substances have been recognized as mutagenic factors. We have barely begun to delve into this subject—even at the animal experimentation level—and the list of chemical substances known to have a mutagenic effect will certainly become far more complete in the years to come. We still know nothing about the influence of chemical substances on mutability in human beings, but we have reason to assume that their effect on human populations is much greater than is that of the physical factors. Some experimental researchers already feel justified in drawing the conclusion that all carcinogenic substances are also mutagenic (Demerec, Strong). This conclusion is perhaps premature, but meanwhile we must reckon with the possibility that these substances do have a mutagenic effect. Among the substances considered at the present

time to be carcinogenic—and, after all, more or less every individual in a civilized society is susceptible to the effect of carcinogenic substances—are aromatic hydrocarbons, certain azo dyes, aniline, certain synthetics (cellophane), tobacco (tobacco tar), cigarette smoke, the benzpyrene content in the air of large cities and certain alimentary substances like butter yellow. Also coming to mind in this connection are the universal and progressive denaturing of foodstuffs as a result of canned-food consumption and vitamin deficiencies (but also the body's absorption of innumerable substances administered to it for therapeutic purposes), as well as chemical contraceptives and temporary sterilization agents involving the closest possible contact with the germ cells. To be sure, not a single case of injury to a child resulting from unsuccessful contraception with chemical agents has been proved beyond refutation (Gesenius), but this fact still does not rule out the possibility of damage to the genotype by such preventative agents. The detection of such adverse effects, we repeat, will require generations of observation.

We are completely aware of the difficulties involved in research concerning the effect of mutagenic factors in human beings. However, there is no reason to adopt an attitude of resignation. In this field, too, there are ways and means of carrying out important preliminary work. For instance, a universal survey of hereditary diseases in the civilized countries, such as the one called for in the preceding section, and the systematic study of the frequency and distribution of pathologic genes in the various countries and among the various races on the different continents could give us indications concerning the effect of mutagenic factors, if geographical differences exist with respect to the rate of mutation of a gene. Table 1 shows the two hereditary diseases with the highest rates of mutation, thalassemia (4×10^{-4}) and sickle cell anemia (1×10^{-2}). Both diseases are definitely linked with nationality or race factors. Thalassemia appears almost exclusively among Italians, sickle cell anemia among Negroes and mulattoes. However, the distribution of the disease within a nation or race is by no means uniform. For instance, thalassemia is particularly widespread in the Po Delta and in Sicily, and the high rates of mutation have been computed on the basis of such populations with numerous bearers of the trait. If the calculations were based on populations from other sections of Italy, the rates of mutation would be far lower. In such cases, a search should be made for mutagenic factors, even though local differences in the distribution of a pathologic gene need by no means be caused by a different rate of mutation.

Selective Pressure and Counterselection

Individuals who are carriers of a hereditary disease or of a hereditary anomaly are in general more or less at a disadvantage compared to normal individuals in the matter of reproduction, *i.e.*, they are under greater selective pressure. The selective disadvantage is represented by the symbol f in the formula for calculating the rate of mutation. If we postulate the reproductive fitness f, of the normal individual as equal to 1, the f value for the individual with a hereditary disease lies between 1 and 0. If all sufferers from a hereditary disease die before the onset of sexual maturity, f equals 0. In the case of infantile amaurotic idiocy, myatonia and pancreatic fibrosis, children already die in infancy or in early childhood. The diseases in question are inherited recessively and transmitted solely through the phenotypically healthy heterozygotes. In the case of dominant transmission it is likewise often only the homozygous cases which are more or less fatal, as thalassemia and sickle cell anemia, whereas in such cases heterozygotes are merely affected with a harmless form of anemia. The dying off of the heterozygous carriers of dominant characters even before sexual maturity would make transmission completely impossible and the mutated gene would already

be eliminated in the generation in which the correlated character made its appearance. In the case of most dominant hereditary diseases at least some of the heterozygotes reach the age of reproduction. For instance, it is true that in chondrodystrophy 80 per cent of the trait carriers die during their first year of life, but beyond this age viability is normal. To be sure, in the latter event his chances of reproducing are nevertheless still limited inasmuch as a crippled chondrodystrophic dwarf does not have the same prospects of finding a marriage partner as a normal individual. In the case of Pelger's anomaly, which, at least in heterozygotes, represents a harmless blood variant, the selective disadvantage of the heterozygotes compared with the non-Pelger cases is slight, amounting to only 5 per cent.

It is obviously clear that the frequency of a hereditary disease whose carriers are more or less seriously exposed to extinction before they have reproduced can remain unchanged in the population only when the number eliminated is balanced out by new mutations. The question as to how it happens that mutation and elimination balance each other out and, consequently, that an equilibrium is established in the population has been answered very satisfactorily by Stern with an example which is cited here (Table 3).

TABLE 3

(According to Stern)

Frequencies of a pathogenic dominant allele *A* in successive generations. Rate of mutation, 1: 100,000. Size of population: 1 million. Reproductive fitness of *A* = 0.5.

Generation	Normal Allele *a*	Pathogenic Alleles *A*		
		Newly Mutated Allele *A*	Remaining Allele *A* from Previous Generations	Total Number of *A* Alleles
0	2 mill. (*)	—	—	—
1	"	20	—	20
2	"	20	10	30
3	"	20	10+5	35
4	"	20	10+5+2.5	37.5
5	"	20	10+5+2.5+1.25	38.75
–	–	–	–	–
–	–	–	–	–
∞	"	20	10+5+2.5+1.25+...	40

(*) More exactly: 2 million *a* alleles minus the number of *A* alleles in every generation.

In a population of 1 million individuals per generation, a pathogenic allele *A* may appear with a mutation rate of 1:100,000 per gene, and its reproductive fitness will amount to only half that of the normal allele *a*. If the pathogenic allele was not yet present in the initial generation and appeared with the indicated frequency as a new mutant from the following generation onward, and with the elimination of half the *A* alleles in each generation in accordance with the table, a state of near equilibrium would be reached after only 4–5 generations.

However, the picture is basically altered when the carriers of hereditary diseases, who previously died prematurely, are kept alive by successful therapy and thus enabled to reach sexual maturity and to reproduce. In this manner the selective pressure is moderated, if not completely eliminated, *i.e.*, a counterselection sets in. Reproductivity *f*, which amounted to 0 or to a fraction of 1, approaches the value 1 of normal individuals. There is no doubt as to the very great successes achieved during the last half century in the treatment of many hereditary diseases. Here, we shall cite only a few examples.

The pathological condition of cleft lip-jaw-palate is one of the most frequent deformities of the body, manifesting itself in various forms ranging from the simple cleft of the upper lip, *i.e.*, harelip, to a complete cleft in the roof of the palate, *i.e.*, cheilognathouranoschisis. In Germany, 1–2

cases in every 1,000 births have the anomaly in some form or other. Other civilized nations present similar statistics. The anomaly is twice as frequent in the male as in the female sex. As late as the previous century, all children with a cleft palate died. At the present time, operative techniques have been developed to such a degree that the malformation need no longer be fatal. In most cases, the operation leaves only slight externally visible scars, and today the bearer of the deformity has practically the same chance of attaining sexual maturity and reproducing as a normal individual. With a frequency rate of 1:1,000 for this malformation, there are approximately 1,000 deformed children for every 1 million births; as late as the last century most of these would still have been eliminated by natural selection. Even though the cleft lip-jaw-palate is in some cases not the result of heredity, the number of hereditary cases in successive generations is bound to increase as the result of countersection. As a matter of fact, it is reported that the number of cleft lip-jaw-palate cases has doubled during the last century (v. Verschuer).

The same situation prevails in the case of two other very widely distributed malformations of the body, so-called congenital dislocation of the hip-joint and club-foot. Even cases of bilateral dislocated hip-joint have been operated successfully and no longer represent an obstacle to marriage; persons afflicted with club-foot can be "decrippled" by surgery and are likewise no longer at a disadvantage compared to individuals with a healthy heredity.

I should like to mention diabetes mellitus as the classical example of the effect of counterselective measures. Since the introduction of insulin therapy, the life expectancy and functional ability of the sufferer from diabetes mellitus have increased considerably. Whereas previously diabetic men and women were largely infertile, it is now possible, thanks to insulin, not only to eliminate impotence in men and sterility in women patients, but to bring about successful pregnancies through sex hormone treatments. Previously, when female diabetics did actually succeed in becoming pregnant, at least half the children of such mothers died before birth or shortly thereafter. The fact cannot be doubted that there has been an increase in the number of diabetics in the last half century (Pannhorst).

Since the recognition of normal blood transfusions as a very effective therapeutic measure, even hemophilia is hardly any longer a threat to the life of the hemophilic. The first genuine (homozygous) female hemophilic, born of the union of a hemophilic male with a female transmitter, was recently described (Israëls, Lempert and Gilbertson). The pregnancy of this hemophilic woman and the birth of her child proceeded normally: subsequent heavy hemorrhages were successfully controlled by means of blood transfusions.

In nearly every field of hereditary disease similar therapeutic successes have been reported which, both from the standpoint of the patient and that of the attending physician, can only be welcomed. However, as geneticists and eugenists we must not lose sight of the other side of the picture of such counterselection. Referring to Table 3 again, if the reproductive fitness as determined by selective pressure is raised by means of counterselection from $A=0.5$ to $A=1$ (without any change taking place in the mutation rate of 1:100,000), the number of *A* alleles will increase from generation to generation and the number of mutants or hereditary disease cases in the population will increase correspondingly.

To be sure, we still lack all satisfactory data enabling us to arrive at an exact evaluation of the degree and effect of counterselection in the individual hereditary diseases. In this field, too, almost all of the work still lies before us, and in conclusion I should like to cite the phrase with which Curt Stern prefaced his paper at this conference: "Research needed!"

DYNAMICS OF HUMAN POPULATIONS*

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ONE OF THE MOST DISTINCTIVE FEATURES of our age is the rapid multiplication of our species, *homo sapiens*.

The present growth of world population is utterly unique in human history. This can be painfully demonstrated from bits of historical evidence. But a little simple arithmetic will show that this must be true. The present annual world population growth is estimated at well over 30 million and perhaps as high as 40 million a year. Had this *amount* of growth continued throughout the Christian era, there would now be 60–80 billions of us rather than the actual figure of about 2.6 billion. At the present *rate* of growth (which is estimated to be at least 1.2 per cent per year) the entire population of the globe would be descended from a single couple living at the time of Christ. An Argentinian demographer has carried the illustration to its logical conclusion: if the population of two living in the Garden of Eden some 6000 years ago had increased on the average of 1 per cent per year the present human population would be so vast that it would have standing room only, not just on the surface of the earth, but on the surface of a sphere with a radius 14 times the *orbit* of the planet Neptune. Obviously the amount of current population growth could have existed only in brief periods of man's history.

The Growth Potential

The magnitude of the population problem of the modern world therefore is completely new. It is the problem of the enormous growth unleashed by the splendid success of our civilization in preserving human life. The armentorium of modern medicine and public health, applied within the public order maintained by the modern state, have made possible the doubling of the average expectation of life at birth. For Americans and Europeans the expectation is 20 years longer than in our grandparents' generation and 40 years longer than in 17th-century Europe. This is perhaps the greatest material achievement of our civilization.

This achievement took centuries in the West; but in countries more recently undergoing modernization, this is happening much more rapidly—in a matter of decades or even a few years. In Ceylon for example a simple program of systematically spraying all human habitations with DDT resulted in a cut in half in the death rate in the eight years between 1945 and 1953. This program in Ceylon has been carried out with a total expenditure of about two dollars per individual per year on public health.

Comparable achievements in the next decade among the two-thirds of us who live in underdeveloped areas would double the average rate of world population growth actually experienced since World War II. This may not be possible. But with a modicum of peace and prosperity it is a realizable goal in 20 years. Without declines in the birth rate this would mean an average world population growth of about 2½ per cent per year. We are faced with the probability that world population growth will very soon accelerate to 1½ or 2 per cent per year. *Could* and *will* such growth be maintained?

In the broad sweep of history the answer to both questions is unequivocally *no*. In the shorter run, say over the next generation, the answer is probably *yes*.

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Such growth is by definition a transitional phase in the dynamics of human population. It could not have existed for any long period in the past; it cannot exist for any really long period in the future. It is an inexorable law of compound interest that the present growth continued even for a few centuries would literally crowd us off the earth.

At the postwar rate of growth, the world's population will achieve 40 billion in 250 years. This would mean an average density of 750 per square mile (the present density of England and Wales) over the entire land surface of the earth, including tundra, mountains and deserts. At double the rate of recent growth, which is a short-term possibility, this situation would be reached about the year 2065, or a little more than a century from now.

The Choices

Even assuming that resources could be found to feed such masses, birth rates in the next century must fall or our species will face a cramped and penurious existence that few of us would like to contemplate. The longer-range alternative is a return to a grim struggle for existence that would raise death rates to former levels. Barring the early colonization and exploitation of other planets and heavenly bodies, birth rates must fall or deaths from starvation, from disease, and from war must again rise.

But we have a period of grace, perhaps two or three generations, in which to work out a new biological balance. For that period the world may be able to support a rapid rate of population growth through more effective use of resources and without being reduced to a diet of algae and yeast.

Fortunately the species has already started along the path needed to bring about a new and more humane balance of births and deaths. As is now widely known, the great gains in postponing deaths in the advanced countries of the West have been partially matched by subsequent declines in the birth rate.

It is natural that a decline in the birth rate should follow rather than precede the decline of the death rate in demographic evolution.

From time immemorial human beings have had the strongest biological, social and even religious compulsions to "increase and multiply." These compulsions have evoked persistently high birth rates throughout the world. Such reproduction was costly in terms of human wastage, since a large proportion of those born failed to achieve maturity. But high birth rates were necessary if the race were to survive the perils of life in all previous ages. It is the very modern achievements in the postponement of death that make it possible and practical to spare the race the hardships and wastes of uncontrolled fertility. We are also witnessing great advances in the reduction of sterility. The rational control of family size thus has two aspects; first, it eliminates the necessity for irresponsible childbearing among those ill-equipped to provide numerous progeny with a good start in life. Second, it also enables many couples who otherwise would have been denied this privilege to share the duties and pleasures of rearing their own children.

Toward a New Demographic Balance

1. *The West.* About one-third of the human race now exercises a substantial degree of voluntary control of family size. In a number of European countries the reduction of births had reached a point before World War II at which many persons both in Fascist and in democratic countries were becoming worried about the possibility of race suicide. The baby boom following the war dispelled the fears that people, given the means of voluntary control of family size, will necessarily fail to reproduce themselves. In fact, the wide fluctuations in the birth rate in the depression years, during the war, and in the postwar period have concealed a rather stable average family size in the West.

What matters in the long run is not the annual birth rate but the size of completed families. Recent analysis of cohort fertility,

that is, the fertility of women born in the same years and passing through life together, has given us new methods for analyzing fertility trends.[1] Among white women born in the United States in 5-year periods from 1900 to 1925, the average number of children per woman has varied only between 2.3 for the women born 1905–1909 to a maximum of 2.7 for those born 1920–1924. The latter women of course have not completed their normal child-bearing years, but it is possible to make reasonable estimates of their final fertility performance on the basis of their experience thus far. These data indicate that the actual size of American families has not changed nearly so much as the annual birth rates might suggest.

Similar studies in Britain suggest that the average number of children per married woman has remained remarkably stable over the last 25 years at about 2.2 children per woman. This is about 5 per cent below the number necessary for permanent replacement.

It would seem that the industrial West is moving toward a new and more efficient reproduction in which low birth and death rates are roughly balanced in a new demographic equilibrium.

2. *Areas in Transition.* There is every reason to suppose that the huge populations of the underdeveloped areas, given the opportunity, will respond to the same incentives that have brought about the reductions of births in the West. Neither ideology nor great cultural barriers have stopped the decline of births in a country once modern influences have reached the mass of the people. Let me illustrate this, first, from the experience of Russia and second, from the experience of Japan.

The categorical anti-Malthusian doctrines of Communism, backed by the most comprehensive pro-natalist policies in existence, have apparently not been successful in checking very rapid declines in the Russian birth rate since the war. Before World War II the Russians were temporarily successful in checking the very rapid decline of births resulting from abortions in the early 1930's. This success was achieved by the simple expedient of closing down the free public abortion clinics. Since the war, however, the supplements to family wages on behalf of children and the "mother heroine medals" seem to have been ineffective in stopping the spread of the small-family pattern.

According to the population experts from the Soviet Union at the recent World Population Conference in Rome, the present birth rate in the Soviet Union is approximately 24 per thousand population, or slightly less than that in the United States. This represents a drastic decline from the prewar figure of 38 per thousand. If adjustment is made for the concentration of the Russian population in the young adult ages, the current fertility in the U.S.S.R. must be substantially below that in the U.S. When such a decline occurs in bourgeois countries, it is condemned as evidence of the refusal of parents to bring children into a world of capitalistic exploitation.

The case of Japan is equally revealing with reference to the extent to which the small family pattern may cross cultural barriers. Once Japan became predominantly urban and industrial, the traditional forces of Oriental familism and ancestor worship apparently failed to retard the decline of the birth rate. It is interesting to note that aside from fluctuations in the birth and death rates associated with wars, the pattern of vital rates in Japan during the last 35 years has very closely approximated the trend of birth and death rates in England 40 years earlier at a somewhat comparable stage of industralization. By 1953 the birth rate in Japan was 21.5, well below that of the United States and rapidly approaching European levels.

[1]See P. K. Whelpton. "Future Fertility of American Women," *Eugenics Quarterly*, Vol. 1, No. 1, March 1954.

The specific means used to restrict family size may differ from country to country: in Ireland, through late marriage; in Western Europe, generally, by birth control; in Japan, by abortions, which Japanese experts report now number over one million a year, despite growing efforts by the Japanese Government to introduce less drastic methods of family limitation; and, in Puerto Rico and increasingly elsewhere, by post-partum sterilization of women in hospitals, at the request of the women concerned and generally following the delivery of their fourth or fifth child. The birth rate has declined wherever people have become literate, urbanized, and free of the debilitating psychological and physical effects of the major epidemic diseases.

Population Growth and Economic Progress

There is every probability that all segments of the human race will acquire the small-family pattern in the event of major transformation of their societies through industrialization and modernization. The problem is rather the degree to which and the speed with which this will occur. In some cases population growth itself may so handicap economic progress as to prevent the kind of material progress associated with birth declines.

This is difficult for many in the underdeveloped areas to understand. Population growth per se has been quite properly regarded historically as a sign of progress and prosperity. Indeed, the two, economic growth and population growth, have gone together. And for the first time hope is being held out that the human race as a whole, not just a single class or master race, can be freed from the degradation of grinding poverty and needless suffering. This hope is justified by technical achievements and by the rising capacity to produce. Probably the cornucopia-minded are correct in asserting that the world could meet these expectations for its present numbers. But a large part of the economic gains must each year be diverted to provide new places at the world's table rather than to improve the fare of those already here. To use a different figure of speech, some countries, like the Red Queen in "Alice Through the Looking-Glass," must run faster and faster simply to stay in the same place.

The "world population problem" turns out on inspection to be a series of regional and national problems. Much more important than the total resources theoretically available in the world as a whole are the specific resources available in relation to the populations of specific countries and regions. In fact even here the oft-discussed framework of the relation of people to resources offers a somewhat inadequate statement of the problem. Quite as important as the physical resources in relation to the population are the crucial intervening variables that determine how effectively the physical resources are used and converted to meet the needs of the populations. The equations of technology, social organization, and especially political stability may be quite as important in determining levels of living as the stock of physical resources.

Furthermore, the future birth rates are not matters that will be decided in the long run by governmental policies. The future trend of the birth rate in the underdeveloped areas, as in the industrial West, will be a matter of choice and action of millions of individuals. These are only within limits amenable to the influence of public policy calculated to change population trends.

The real question is the extent to which individual families will achieve the right and the ability to improve their lot by control of their own destiny. People will be guided, not by abstract ratios of population to resources, but by the extent to which individual and familial aspirations can be met by limiting family size. The actual population trends are not really so responsive to poverty as such as to the changing motivations of individuals. Where economic aspirations outrun the means of satisfying them, as is increasingly characteristic of people in underdeveloped areas,

it is reasonable that parents should turn to family limitation as a means of providing more opportunities for the children they do have. Consequently demography has become increasingly concerned with the socio-psychological aspects of fertility as opposed to purely economic motivations.

The differing stages in economic and social development existing in the world have given rise to differential population growth among regions. Many of the world's tensions and frictions may be traced back to the disequilibrium arising from the different stages of economic and demographic evolution achieved in the several parts of the world.

Forecasts

Let us turn to present population growth and the outlook for future growth in the several major regions of the world. For this purpose we may use recent forecasts prepared by the Population Division of the United Nations relating to the period 1950–1980.[2] These materials are presented in graphic form in Figures 1 and 2, and the basic data is in tabular form in Tables 1 and 2.

Figure 1 is intended to give historical perspective, illustrating the momentum and acceleration of *absolute* population growth in the world and its two great subdivisions: Asia-Africa, and the European settlement area, which includes Europe and the U.S.S.R., the Americas and Oceania. Since 1650 there has been a great expansion of the European population. In some periods this has exceeded even the absolute amount of growth in Asia and Africa, but the latter area has never lost its clear predominance in numbers. Current and foreseeable trends will widen this predominance.

The extent of this divergence will depend much on the situation in China. Until very recently it was generally accepted that the population of China was under 500 million and that it was growing little if at all. The United Nations estimates incorporates this assumption in their forecasts. Only last month, however, reports from the first modern census in China, taken in 1953, indicate a population of not 500 million but close to 600 million increasing at 2 per cent per year. If these latter figures for China were used in the projections, the world estimate for 1980 would be close to 4 billion rather than the 3.6 billion shown on this chart.

Figure 2 shows the United Nations forecasts in greater detail, this time on a logarithmic scale in which parallel lines indicate equal rates of growth, rather than equal amounts of increase.

All regions are growing and will continue to grow barring a major catastrophe. It is natural that demographic evolution should have proceeded further in Western Europe, the birthplace of modern industrial civilization. But despite somber predictions made by myself and others a decade ago no population decline in Europe is yet in prospect. In fact there is some suggestion that the very appearance of decline, as in France before the war, will bring about reactions in public policy and private attitudes sufficient to restore a moderate rate of growth.

Eastern Europe is the one major region in which the demographic losses of World War II are discernible in the population curve, partly of course as a result of mass expulsions. If very recent information on the rapidity of the decline in the birth rate in the U.S.S.R. and the satellite countries is accurate, the United Nations forecasts for this area are too high.

In overseas Europe, *i.e.*, in the United States, in Canada, in Australasia, and in temperate zones of South America, population growth is still rapid and above the world average. While present growth rates may not be maintained, we may expect continued growth at a less rapid pace, both

[2]United Nations, Population Division, *Framework for Future Population Estimates 1950-1980, By World Regions.* Document E/CONF. 13/126 (mimeographed) presented at the World Population Conference, Rome, September, 1954. The estimates given in this document are provisional and may be revised for final publication.

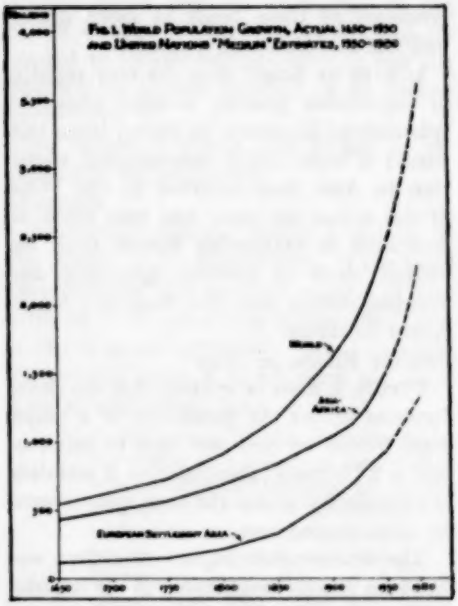

FIG. 1. WORLD POPULATION GROWTH, ACTUAL 1650–1950 AND UNITED NATIONS "MEDIUM" ESTIMATES, 1950–1980

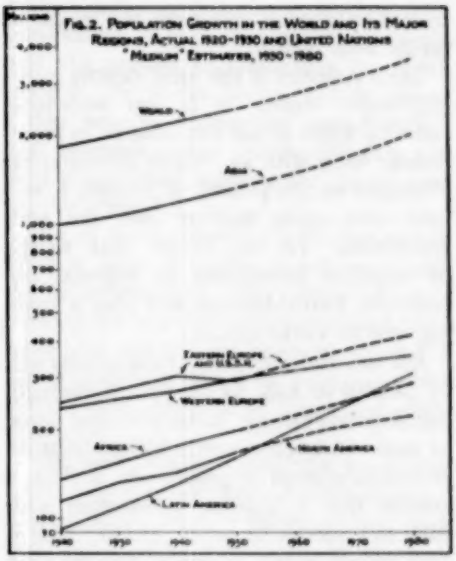

FIG. 2. POPULATION GROWTH IN THE WORLD AND ITS MAJOR REGIONS, ACTUAL 1920–1950 AND UNITED NATIONS "MEDIUM" ESTIMATES, 1950–1980

TABLE 1

WORLD POPULATION GROWTH, ACTUAL 1650–1950 AND UNITED NATIONS "MEDIUM" ESTIMATES, 1950–1980

	(IN MILLIONS)		
Year	*World*	*Asia-Africa*	*European Settlement Area*
1650	545	427	118
1750	728	570	158
1800	906	687	219
1850	1171	836	335
1900	1608	1035	573
1920	1834	1133	701
1930	2008	1224	784
1940	2216	1350	866
1950	2454	1518	936
1955	2603	1605	998
1960	2769	1706	1063
1965	2951	1822	1129
1970	3153	1959	1195
1975	3378	2117	1262
1980	3628	2300	1329

Data 1650–1900 adapted from Carr-Saunders, *World Population*, 1936, p. 42

1920–1940 from United Nations, *The Determinants and Consequences of Population Trends*, 1953, Population Studies, No. 17, p. 11

1950–1980 from United Nations Population Division, *Framework for Future Population Estimates*, 1950–1980, by World Regions (Mimeographed), 1954. All data for East and West Europe in Table 2 refer to post-war areas.

TABLE 2

POPULATION GROWTH IN THE WORLD AND ITS MAJOR REGIONS, 1920–1950 AND UNITED NATIONS "MEDIUM" ESTIMATES, 1950–1980 (IN MILLIONS)

Year	*World*	*Asia*	*Africa*
1920	1834	997	136
1930	2008	1069	155
1940	2216	1173	177
1950	2454	1320	198
1955	2603	1394	211
1960	2769	1482	224
1965	2951	1584	238
1970	3153	1705	254
1975	3378	1846	271
1980	3628	2011	289

Year	*West Europe*	*East Europe and U.S.S.R.*	*North America*	*Latin America*	*Oceania*
1920	238	248	115	92	9
1930	255	276	134	110	10
1940	272	305	144	132	11
1950	298	295	168	162	13
1955	309	316	179	181	14
1960	319	337	190	202	15
1965	329	358	200	226	16
1970	339	379	209	251	16
1975	348	399	217	280	17
1980	358	419	223	312	18

from immigration and from the excess of births over deaths.

Latin America is the most rapidly growing major region. It is now surpassing America north of the Rio Grande in population. Even with an orderly demographic evolution on the pattern of Europe, it will have very rapid increase over the next generation. To the extent that weight of numbers contributes to regional importance, Latin America will play a growing role in world affairs.

But the biological fate of the species will be decided in Asia, which now, as throughout recorded history, is the principal home of man. Only catastrophe will prevent an enormous growth of population in Asia, a growth that is gaining momentum with each new success in public health. This is both necessary and desirable. But the most rapid present and potential growth often is in areas least well endowed in terms of physical and cultural resources to meet the needs of an expanding population.

The United Nations forecasts a population of 2.0 billion in Asia in 1980, or 2.3 billion if we adjust for the new reports of population growth in China. I have already mentioned that almost 600 million people in China are now reported to be growing at the rate of 2 per cent, or about 12 million persons, per year, the difference between the reported birth rate of 37 and the reported death rate of 17 per thousand population. It is difficult to imagine but that such a growth is a very serious handicap to economic development in so crowded a land under whatever political system.

On the other hand, population growth in such crowded countries of the free world as India and Indonesia imposes a heavy handicap on their development by democratic methods. Capital formation at best involves hardships in such poor countries, and the task is greatly increased if economic gains must be consumed in feeding several more million people each year. Population growth may itself contribute to frustrations pushing the people and governments of these lands to more drastic political and economic methods.

It is to be hoped that the very rapidity of population growth, brought about by splendid achievements in saving lives, may herald a more rapid demographic transition in Asia than occurred in the West. If this is not the case, Asia may never be successful in extricating herself from the vicious circle of poverty, ignorance and over-population that has been her lot in recent centuries.

Possible Effects of War

Finally, it must be evident that the above forecasts ignore the possibility of a major war. While we may not care to think of war as a "normal" phenomenon it certainly is a possibility within the time span covered by these projections.

The demographic impact of modern war has been greatly exaggerated in the popular imagination. While war losses of the two World Wars seriously reduced selected populations, their impact was temporary and local, viewing the world as a whole. Their impact was negligible in retarding the forward march of world population growth. Aside from the single case of Eastern Europe one would have to look very closely on the two figures to detect any effects of the two World Wars.

This does not in any way minimize the personal tragedy or horror of war. It merely reflects the fact that the social and biological forces leading to world population growth represent basic and powerful forces that were only very temporarily checked by the two World Wars.

Another war, fought with the arsenal of horrible new weapons, might of course be far more disastrous to the species. But only about 5 per cent of the world's population lives in its 60 odd urban agglomerations of over one million inhabitants. The destruction of all our major cities would not directly destroy a large part of the human race. For that matter four or five normal years of world population growth would completely replace the population of the

United States and six years that of the Soviet Union. These remarks are not intended to be comforting—only to put the problem of human survival in its proper perspective.

In closing I would like briefly to recapitulate the argument.

Summary

Modern population growth is unique in the history of the human race. It has been unleashed by the splendid success of our civilization in preserving human life. But it cannot go on indefinitely. It is inevitably a transition stage in which there are three general possibilities open to us:

1. A reduction of the birth rate in the world as a whole, to establish a new biological balance of births and deaths at levels commensurate with the improved standards of health and physical well-being;
2. Increasing congestion of human populations that must ultimately result in a return to the high death rates and wasteful biological balance characteristic of all previous human history;
3. Periodic decimation of the population through war.

The choice must be made decisively within the next two or three generations. At the present time we seem to have embarked on the first course. The one-third of the human race living in the more advanced Western countries now to a large extent controls its fertility, with resulting declines in the birth rate. The fears that such declines would result in "race suicide" have proven unfounded. Western populations seem to be approaching a new, more efficient and more humane balance of births and deaths.

The forces leading to this demographic revolution appear to be stronger than either political doctrine or cultural barriers. Such is the conclusion that may be reached from observation of the rapid decline in births and the present comparatively low birth rates in the Soviet Union and in Japan. Other peoples undergoing modernization will probably accept the small-family pattern if economic development can proceed rapidly enough.

But in the meantime population growth itself is often a serious handicap to economic development. The present efforts to develop the so-called underdeveloped areas would be much more likely to succeed if the demographic transition were to precede rather than follow the major economic transition.

The possible meaning of these qualitative statements in terms of possible future populations of the several major regions have been illustrated in the charting of the population estimates made by the United Nations. These forecasts indicate continued population growth in every major region of the world, at least up to 1980. The greatest absolute population growth will probably take place in Asia. The future of the species may well hinge on how rapidly Asians acquire the small-family patterns now adopted in the West, in the Soviet Union and in Japan. The most rapidly growing area is Latin America, and to the extent that bulk of population is a factor in the relative weight of regions in world affairs, the importance of Latin America will substantially increase.

Wars more terrible than those of the past two generations could drastically alter these prospects. But equally crucial to the future of the human species is the success and speed with which the two-thirds of us living in underdeveloped areas achieve the economic and social transformation these countries are now struggling to attain.

HEREDITY AND DIABETES

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BY THE BEGINNING OF this century most investigators were agreed that heredity plays a large role in the causation of diabetes mellitus. Today, no one rises to challenge Joslin's statement that, "Heredity is the basis of diabetes" (2).

The recognition that heredity is important in the causation of diabetes makes it possible to provide answers to the oft-repeated question of "How likely am I to develop diabetes?". The availability of excellent measures for the control and perhaps the prevention of diabetes makes it urgent that the question be answered.

The answer depends on many variables. This paper presents answers taking into account the variables of age and family history relative to diabetes.

Investigations based on large numbers of carefully collected histories show that diabetes is about twice as frequent among the sibs (sisters and brothers) of diabetic patients who have a diabetic parent as among the sibs of diabetic patients who do not have an affected parent. Table 1 shows the data from four recent studies, each of which examined the families of more than 1000 patients. Such data suggest recessive inheritance, and it has been shown that such an hypothesis will explain these data (3). We may conclude, therefore, that susceptibility to diabetes is inherited via a simple recessive gene which we shall symbolize as "d". *Individuals who are genetically liable to diabetes are "dd". Those not genetically liable to diabetes are "Dd" or "DD".*

Estimates based on two different sets of data indicate that about 5 per cent of the population of the United States is homozygous for the gene determining susceptibility of diabetes, that is, are "dd" (4). As a consequence of the variability in age at onset and in the severity of the disease, only about 1 per cent of the population is recognized to be diabetic (2). It appears from various studies that an additional 1 per cent of the population is diabetic but not recognized to be so (7). We must conclude, therefore, that 60 to 80 per cent of those who are genetically liable to diabetes, that is, who are "dd", are not recognized by present routine methods of examination.

The following paragraphs show how these facts may be applied to estimate the probability that a relative of a diabetic individual will be genetically liable to diabetes.

TABLE 1

THE FREQUENCY IN PER CENT OF DIABETES AMONG THE SIBS OF DIABETIC PATIENTS WITH NEITHER PARENT OR ONE PARENT DIABETIC.

Source of Data	Harris (1)	Thompson & Watson (5)	Steinberg & Wilder (4)	von Kries (6)
Neither parent diabetic	3.5	7.7	4.7	3.2
One parent diabetic	11.7	15.3	11.4	8.9
Number of families studied	1241	1631	1981	1305

The probability that a sib of a diabetic individual is genetically liable to diabetes.

A diabetic individual is, as we have seen, genetically "dd". Therefore, each of his parents must have contributed one "d" gene to his genotype (genetic make-up). Consequently, the mating which gave rise to him must have been one of the following three types, where "d" represents the gene which when present in double dose (homozygous) leads to genetic susceptibility to diabetes, and "D", the gene which when present in single or double dose leads to non-susceptibility to diabetes.

TABLE 2

		Per cent of "dd" offspring
1.	Dd × Dd (neither parent genetically liable to diabetes)	25
2.	Dd × dd (one parent genetically liable to diabetes)	50
3.	dd × dd (both parents genetically liable to diabetes)	100

If one is concerned about the sibs of a diabetic, he must first determine if none, one, or both of the patient's parents are diabetic. Because diabetes may occur at any age, parents stated to be non-diabetic may nevertheless develop diabetes at a later age. That is, some non-diabetic parents may be genetically liable to diabetes ("dd"). This introduces an error into our predictions. However, for the present illustrative purposes we will ignore this error.

Having determined which of the patient's parents is diabetic, we have two types of questions to answer: (a) What proportion of his sibs will be observed to be diabetic; and (b) What proportion of his sibs are genetically liable to diabetes?

A precise answer to (a) cannot be given at this time. The number of observed diabetic sibs is a function among other things of the age of the diabetic patient and the method of examining the sibs. More sibs will be found to be diabetic if glucose tolerance tests are done than if individuals are merely asked whether they are diabetic.

Reference to Table 1 will show that rather wide differences in frequencies of affected sibs have been reported by different investigators. There were too few patients with both parents diabetic to derive meaningful values for the frequencies of affected sibs. All these data are based on information derived by questioning the patient concerning his relatives; therefore, the frequency of affected sibs most probably is too low. Hence, it does not seem very useful to quote any frequencies for clinical use. For general survey data, values of 6, 12 and 25 per cent of affected sibs when none, one, or both parents, respectively, are diabetic seem reasonable.

The answer to (b) is relatively simple and for clinical purposes the more important. If neither parent is diabetic, about one-quarter of the patient's sibs will be genetically liable to diabetes; when one parent is diabetic about one-half of the sibs will be; and when both parents are diabetic all the sibs will be genetically liable to diabetes (see Table 2).

While it was permissible for illustrative purposes to ignore the possibility that a non-diabetic individual may be "dd" (that is, genetically liable to diabetes), this possibility must be considered when estimating the probability that an individual may be genetically liable to the disease.

Consider the case of a young couple with a five-year-old diabetic child. Neither of the parents is diabetic, but both are less than 40 years of age. If we were to conclude that neither parent is "dd" (because neither is diabetic) the probability, as we have already seen, that any other child of theirs would be "dd" is 25 per cent. However, less than 30 per cent of diabetics become diabetic before 40 years of age. Therefore, there is a considerable chance that one or both parents is "dd" even though neither is diabetic. Hence, a prediction based on the assumption that neither parent is "dd" will be too low.

A better estimate of the probability that other children of these parents will be "dd"

may be calculated. The basic requirements are an estimate of the frequency of the gene "d" and an estimate of the probability that a non-diabetic parent or grandparent may be "dd".

The frequency of the gene "d" has been estimated (4). The probability that a non-diabetic individual may be "dd" depends, among other things, upon the individual's age. For practical purposes, only three situations need be considered when an estimate is being made of the probability that a sib of a diabetic will be diabetic.

1. The parents are old, and therefore there is only a small probability that non-diabetic parents are "dd". In this situation it may be assumed that none of the non-diabetic parents or grandparents may be "dd". This is equivalent to the situation we have already considered. (See Table 2).

2. The parents are less than 40, but the grandparents are over 59. The non-diabetic parents have a considerable chance of being "dd", while the non-diabetic grandparents have a relatively low probability of being "dd". In this situation, we shall assume that the non-diabetic parents may be "dd" and that the non-diabetic grandparents may be "Dd" or "DD" but not "dd".

3. The parents and grandparents are young, and therefore the former have a high probability of being "dd" and the latter a somewhat lower but still considerable probability of being "dd". In this situation, we will assume that non-diabetic parents and grandparents may be "dd".

Table 3 shows the results of the calculations based on these assumptions. The frequencies under column (a) (assumption "a") are those we have already considered. The frequencies under columns (b) and (c) are essentially the same; hence, for practical purposes if the parents are young, values of 35, 60 and 100 per cent may be used when neither, one or both parents, respectively, are diabetic.

The probability that a non-diabetic individual is genetically liable to diabetes.

The physician or geneticist is often asked by a non-diabetic person what are the chances that he will become diabetic. As we have seen, the answer has to be given as the probability that the individual is genetically liable to diabetes rather than as the probability that he will become diabetic.

It will readily be seen that the probability that an individual will be "dd" (genetically liable to diabetes) depends upon which of his relatives is diabetic and upon his age. Usually, the question is asked about a young person. When this is so, the parents are young and the grandparents may be young. Hence, the usual situation will be equivalent to situations 2 and 3 of the previous section. If the person is older, he usually asks the question because he has a diabetic sib or parent(s). In which case, the answer can be found in the proper row of column (a) of Table 3. For example, if neither parent is diabetic but a sib is, the probability is 25 per cent that the questioner is "dd". If one parent and a sib are diabetic the proba-

TABLE 3

PROBABILITY IN PER CENT THAT A SIB OF A DIABETIC INDIVIDUAL WILL BE GENETICALLY LIABLE TO DIABETES.

	ASSUMPTIONS		
Number of Diabetic parents	(a) Non-diabetic parent may *not* be "dd"	(b) Non-diabetic *parents may* be "dd" but non-diabetic *grandparents* may *not* be "dd"	(c) Non-diabetic parents and grandparents *may* be "dd"
Neither	25	35	37
One	50	59	61
Both	100	100	100

bility is 50 per cent, and if both parents are diabetic the probability is 100 per cent (Table 3). If, however, only one parent is diabetic and no sib is affected, the answer must be sought in Table 4 or 5.

Detailed calculations of the probability that individuals with various combinations of affected relatives will be genetically liable to diabetes based on assumptions (b) and (c) yield similar values (Table 4). Therefore, it is not useful to consider them separately. Furthermore, the computed values are at best only approximations. Therefore, for practical purposes the probabilities may be grouped and the detailed calculated values reserved for technical studies. The grouped values are shown in Table 5.

To use Table 5, first determine which relatives are diabetic. It is well to remember that the more distant the relationship of the diabetic relative, the lower the probability that the individual is genetically liable to diabetes. If a first cousin or one grandparent is diabetic, the probability that an individual is "dd" is not more than 20

TABLE 4

PROBABILITY IN PER CENT THAT AN INDIVIDUAL WILL BE GENETICALLY LIABLE TO DIABETES IF HE HAS ONE OR MORE DIABETIC RELATIVES†.

Diabetic Relatives	*Range of probability* *Lower value**	*Upper value***
1. One grandparent	11	14
2. Two grandparents (not spouses)	35	37
3. Two grandparents (spouses) Note this is equivalent to one parent diabetic (see 6)	18	22
4. Uncle or aunt	9	14
5. First cousin	6	9
6. One parent (see 3)	18	22
7. One parent (say father) and one grandparent (maternal)	59	61
8. One parent and a sib of the non-diabetic parent	50	61
9. One parent and first cousin on non-diabetic parent's side	34	42
10. One parent, and a parent and sib of the non-diabetic parent	75	80

†Relatives refer to grandparents, aunts, uncles and first cousins. If a sib is diabetic, use Table 3.
*Non-diabetic *parents may be "dd"* but non-diabetic grandparents may not be "dd".
**Non-diabetic parents and grandparents may be "dd".

TABLE 5

PROBABILITY THAT AN INDIVIDUAL WILL BE GENETICALLY LIABLE TO DIABETES IF HE HAS ONE OR MORE DIABETIC RELATIVES†.

Probability that person is genetically liable to diabetes*	Diabetic Relatives
Up to and including 20 per cent	1. First cousin 2. Uncle or aunt 3. One grandparent 4. Two grandparents (spouses) or one affected parent
30 to 40 per cent	1. Two grandparents (not spouses) 2. One parent and first cousin on non-diabetic parent's side
50 to 80 per cent	1. One parent and a sib of the non-diabetic parent 2. One parent and a parent of the non-diabetic parent 3. One parent, and a sib and a parent of the non-diabetic parent

†Relatives refers to parents, grandparents, aunts, uncles and first cousins. If a sib is diabetic, use Table 4.
*Within each group the relatives are listed so as to yield an increasing probability that the person is "dd". Thus, an individual with only a first cousin diabetic (1 of the first group) has the lowest probability of being "dd" while a person with one parent, (3 of the last group) has the highest probability of being "dd".

per cent. If a parent and a sib of the non-diabetic parent are diabetic, the probability that an individual is "dd" is between 50 and 80 per cent.

An important use of the type of information presented in Tables 3, 4 and 5 is to estimate in what detail and how often to examine a given person for diabetes. Clearly, the greater the risk for the individual, the more rigorous the preventive measures one is willing to undertake. It is likely that everyone will agree that persons with risks of over 50 per cent should be provided with maximum preventive measures. Probably most will also agree that those with risks of 30 to 40 per cent should be closely followed. Wider divergences of opinion will be encountered when the group with less than 20 per cent risk is considered. At any rate, in each instance, the decision will have to be made by the physician in consultation with the patient.

Prediction of the age at onset of diabetes.

It has been claimed that on the average diabetes will occur in the child of a diabetic at an age 20 years lower than that at which it occurred in the parent and that the child is no longer liable to diabetes when it has passed the age at which the parent became diabetic. This phenomenon is referred to as anticipation.

About two-thirds of diabetic patients with a diabetic parent develop their diabetes at an earlier age than the parent. Analysis of such data, however, has shown that there is no causal relationship between the age at onset of diabetes in parent and child (3). Hence, there is no reason to believe that a child is no longer liable to diabetes when he has passed the age at onset of his diabetic parent. On the contrary, the risk may be quite high if the parent was young when he became diabetic.

A correlation betwen the age at onset of diabetic sibs has been reported (1, 4). The correlation is low, however, and there is reason to believe it is not of clinical significance. Hence, the age at onset of diabetes in a sib has no prognostic value.

We must conclude that at the present time there is no method of predicting when a person who is genetically liable to diabetes will become diabetic.

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CLINICAL IMPLICATIONS OF GENETIC SUSCEPTIBILITY TO DIABETES MELLITUS

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In the article on Heredity and Diabetes on page 26, Arthur Steinberg has given an excellent answer to the question, "How likely am I to develop diabetes?" He has presented risk figures specifying the probability that an individual may be genetically susceptible to diabetes mellitus if he has one or more relatives known to have had this disease. The next question that might be asked is, "If I am susceptible to diabetes, what can I do about it?"

Steinberg has pointed out that for every known diabetic person under medical treatment in the United States, there is another person who is clinically recognizable but who has not yet been diagnosed by a physician, and three other persons who are genetically susceptible but who cannot be recognized as prediabetic by present routine methods of examination. Our present understanding of this disease indicates that two factors must be present before an individual will become ill with clinically recognizable diabetes. First, the individual must be genetically susceptible, and about five per cent of our population are susceptible. Second, he must encounter certain environmental factors which will precipitate clinical disease in a susceptible individual. This implies that a person who is genetically susceptible may be permanently injured by environmental factors that are quite innocuous to a non-susceptible individual. This concept may be summarized as follows, using Steinberg's designation of the susceptible genotype as 'dd':

Susceptible Genotype — dd + Environmental Stress = Clinical Diabetes

As most of us do not have the privilege of choosing our ancestors, we cannot change our genotype or susceptibility status. We can control our environment to some extent, however, and the prevention of disability from diabetes must be based on the recognition and avoidance of the environmental stress factors. Unfortunately, our knowledge of these factors and how they act is still far from complete. Yet it is still of considerable advantage to a susceptible individual to take advantage of even incomplete knowledge concerning prevention.

The environmental factor which has the highest known correlation with clinical diabetes is obesity. Many studies have shown that persons who are overweight are much more likely to develop diabetes than are persons of normal or subnormal weight. It is also a well-known medical observation that the severity of clinical diabetes may be lessened by weight reduction in obese diabetics. A physician may often control a mild obese diabetic for several years without the use of insulin by reducing the diabetic's weight and controlling the diet. Therefore, any individual with a family history of diabetes should make every effort to control his weight and to avoid obesity.

It seems apparent that infections also play some part in the development of diabetes, but their role is not entirely clear. Many diabetics are first recognized by the physician when they appear for treatment of a boil, carbuncle, or other infection which tends to spread or persist. It has also long been known that any infection in a known diabetic is a medical emergency. In the presence of infection the insulin requirement of the body is increased, and a diabetic with an infection usually requires an increased dosage of insulin. The insulin requirement is reduced when the infection is eradicated. For these reasons, any person

who is probably susceptible to diabetes should take every precaution to avoid infections, and should seek prompt and effective medical treatment if any infection should appear. The potential diabetic should also beware of chronic low-grade infections, such as abscessed teeth, recurring urinary tract infections and the like.

The possible role of the diet in precipitating diabetes in susceptible persons has been the subject of some disagreement among physicians. Some feel that a high fat intake may be a significant stress factor, while others feel that a high carbohydrate diet is potentially dangerous. All agree, however, that a susceptible person is safest with a well-balanced normal diet, and that he should avoid any sort of food fads.

The best possible preventive measure in diabetes, as in many other diseases, is the periodic health examination by the family physician. A genetically susceptible person should place himself under the care of the physician of his choice, and inform the physician of the pertinent family history of diabetes. Physical examination, with examination of the urine for sugar, should be done at intervals recommended by the physician, usually every 6 to 12 months. The glucose tolerance test, which measures the ability of the body to utilize a specified amount of sugar, may be used by the physician when he finds it necessary. Even if diabetes cannot be completely prevented in a given individual, early diagnosis and prompt treatment can do much to prevent the more serious complications of the disease.

INSTITUTIONAL PATTERNS FAVORING HIGH FERTILITY IN UNDERDEVELOPED AREAS

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PRACTICALLY ALL OF THE world's underdeveloped areas, embracing something like three-fourths of the world's population, still have high birth rates, that is, more than 30 births per 1000 inhabitants annually and more than 4 births per woman during her reproductive life. In fact, the rates in many underdeveloped areas today are about as high as they have ever been.

In explaining why the rates are so high, we have to ask two questions: First, why were birth rates high in the past? Second, why are they that way now?

The answer to the first question is found, interestingly enough, in the death rate. Until twenty to eighty years ago, depending on the area in question, death rates were extremely high by modern standards. The underdeveloped societies therefore had to have a high fertility to match their high mortality, else they would not survive. Probably many societies in the past failed to survive, their members being killed off faster than they could reproduce. The societies we know about today are necessarily the ones that did survive. They did so because they evolved an institutional structure having an incentive system strong enough to induce their people to reproduce abundantly.

In recent times, however, the necessity imposed by a high mortality has tended to disappear. The death rate in most underdeveloped areas has been declining for a considerable period, and in many it has dropped rapidly in recent years, often faster than it ever did in the now industrialized countries. As a result, many of these areas have today a death rate almost as low as that of industrial nations. In Ceylon, for example, the crude death rate fell by 43 per cent in four years (it was 22.0 per 1000 in 1945, and 12.6 in 1949—and had reached 11.6 in 1951). In Puerto Rico it declined by 46 per cent during the ten years from 1940 to 1950, the rate now resembling that in continental United States; and during the same decade in Formosa it declined by 42 per cent. Comparable reductions have been experienced in parts of the British Caribbean and in parts of Latin America and Africa.

The phenomenally rapid drops in mortality in recent years have generally come on the heels of longer but less spectacular declines in the past. Consequently, our second question is peculiarly relevant—why, in the absence of the necessity that once existed, has the institutional structure of economically retarded areas continued to support a high rate of reproduction?

In beginning an answer to this second question, one must recall that the underdeveloped regions are still in the peasant-agricultural stage of development.[1] This is the stage of economic progress that most of them have been in for many centuries, the stage to which their institutional structure

[1]To be clear as to what is meant by "underdeveloped," we draw the line in terms of the occupational structure. A country with more than 50 per cent of its gainfully employed males occupied in agriculture, fishing, and forestry, we designate as underdeveloped. On this basis, three-fourths of the world's people and three fourths of its area are in countries in this category. See the writer's paper, "Population and the Further Spread of Industrial Society," *Proceedings of the American Philosophical Society*, Vol. 95 (Feb. 15, 1951), pp. 8–19. For the most part the underdeveloped societies are not primitive. Only a small portion of the world's inhabitants live in societies without any literacy and without other accoutrements of modern civilization.

is accordingly well adapted. The rise of industrial nations elsewhere in the world has had an impact on the less advanced areas; it has brought commerce and political change, and it has brought, as we have seen, a marked decline in mortality. But it has not fundamentally altered the agrarian character of the society and to this extent has not forced a change in the institutional structure. Supported by time-honored agrarian conditions, the social organization has retained many of its elaborate mechanisms for inducing a high rate of reproduction. It has done so even though a high birth rate, once functional, has now become strictly disfunctional.

To push the inquiry further, we must try to understand the particular institutional patterns which, in agrarian societies, give rise to this high but disfunctional fertility. Important and clear-cut as the problem is, it has been the subject of surprisingly little research, with the result that misleading theories still persist. Furthermore, since the backward areas embrace cultures of great diversity, students of social structure have been overly impressed and distracted by cultural differences among these areas, overlooking the basic uniformities underlying the surface variations. In other words, if nearly all underdeveloped areas have in common a high fertility, the mechanisms by which they reach this result doubtless also have some things in common. It thus seems wise to look for the deeper uniformities.

In analyzing the institutional factors responsible for fertility, one finds the main key in the family, for human society accomplishes the function of bearing, nourishing, and socializing children primarily through the universal instrumentality of the nuclear family.[2] It is through the relations of the nuclear family to the rest of society, then, that we can expect to find the social factors controlling the level of fertility.

Effect of the Composite Family and Joint Household

In primitive and agrarian societies, as is well known, the nuclear family is less independent of the wider kinship structure than it is in industrial societies. Its formation through marriage, its economic position, and the conduct of its members are all governed by elder relatives to a greater degree. In sociological terms, the nuclear family of procreation tends in agrarian societies to be controlled by other kinship groups, notably by the two families of orientation.

One common arrangement in terms of which such control is facilitated is the joint household, which arises when the newly married couple are required to live with the parents of one or the other partner. Such an arrangement is quite prevalent in underdeveloped areas,[3] but even where it is absent the nuclear family tends to dwell close to and be under the surveillance of the in-laws. Furthermore, it is not simply a matter of dwelling arrangements and social control but also a matter of economic solidarity. The joint household and the composite family often function as an economic unit.

Given this subordination and incorporation of the nuclear family by wider kinship groups, several consequences tend to follow which are conducive to abundant reproduction.

1. *The economic cost of rearing children does not impinge directly on the parents* to the same extent that it does where the nuclear family is a more independent unit. With a common household and a joint

[2]The term "nuclear family" is used by Geo. P. Murdock, *Social Structure* (New York: Macmillan, 1949), Ch. 1, to describe the unit consisting of mother, father, and children. This unit has also been variously characterized as the "primary" or "immediate" family, as in the works of Lloyd Warner.

[3]For the 159 societies for which he secured adequate information on residence and inheritance rules, Murdock found 149 to require residence with extended relatives. *Op. cit.*, p. 38. The majority of these societies, 98 in all, required patrilocal residence. It is hard, however, to reconcile his table on p. 38 with that on p. 32, where the proportion of "independent" families is higher.

economy, with three or more generations present, one's own child draws out of the general exchequer, not out of his parents' income alone.

2. *The inconvenience and effort of child care do not fall so heavily on the parents alone.* With grandparents, aunts, uncles, and older cousins in the household, the care of the young children may be so distributed among the entire menage that no particular strain is put upon the parents. In fact, as has often been pointed out, the joint household is an excellent arrangement whereby young mothers, in the prime of life and thus capable of maximum productivity, are freed during working hours for work in the fields or in handicraft, while older women and older children, less productive economically, look after the infants and younger children. Thus the mother's maternal function does not have to compete with her economic function as in an industrial society.

3. *The age at marriage can be quite young,* because, under joint household conditions, there is no necessary implication that the husband must be "able to support a wife and family" before he gets married. In this respect there seems to have been a difference between West European society, even prior to industrialism, and that of most other parts of the pre-industrial world. The historian, Russell, has pointed out that in the Middle Ages there was a tradition linking the nuclear family with a piece of land adequate to maintain the family.

> In each village there were usually a certain number of holdings of similar character which required the efforts of a mature male, physically and mentally; about thirty acres of land together with a quota of animals upon the manor. . . . Obviously only the full holdings could be expected to care for a family satisfactorily in the eyes of the lay population. Thus naturally marriage would be restricted to those who had holdings. . . . The principle of no holding, no marriage, operated as a fairly effective check upon population increase. The conditions of mortality tended to make the average age of marriage for the young men vary between twenty-two and twenty-five years. It also meant that the weak in mind or body were not permitted to marry. . . .[4]

Thus West European society tended to set the nuclear family apart a long time ago — a fact which is borne out by Western legal history, kinship terminology, and courtship custom. As Western peoples became more commercial and more urban, the rule that land is necessary to form a marriage became extended to mean that a job is necessary. In this way, as commercial and industrial positions came to require apprenticeship and training, and as land became scarce, the way was paved for the postponement of marriage to fairly advanced ages.[5] The more one looks into the matter, the more it appears that the structure of the family in Western industrial societies is not wholly a product of urban-industrialism but is in part a product of cultural peculiarities extending back at least into Medieval times. In fact, it can be argued that the West European family structure was one factor in the origin of the industrial revolution in Northwestern Europe.

Family organization in non-European agrarian societies, however, is different from that of pre-industrial Europe. Especially in Asia, it often embodies the principles of joint residence and joint economic responsibility. Furthermore, the parents in many of these societies are morally obligated to find mates for their children and to marry them at an early age. In the patrilocal joint household the bride simply joins her husband's family and the groom continues to live there. The bride can contribute to the

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[4]Josiah C. Russell, "Demographic Values in the Middle Ages," in Geo. F. Mair (ed)., *Studies In Population* (Princeton: Princeton Univ. Press, 1949), p. 104.

[5]Such postponement, especially noticeable in the latter half of the nineteenth and early twentieth century, was carried to an extreme in Ireland and the Scandinavian countries. See David V. Glass (ed.), *Introduction to Malthus* (London: Watts, 1953), pp. 25-54; Conrad M. Arensberg and Solon T. Kimball, *Family and Community in Ireland* (Cambridge: Harvard University Press, 1940); John Hajnal, "The Marriage Boom," *Population Index*, Vol. 19 (April 1953), pp. 80-101.

joint economy even though young, and the groom is not required to be financially independent. In India, in 1891, nearly a fifth of the girls below 15 years of age, and 89 per cent of those aged 15–19, had been married. The marriage age in India is rising, but as late as 1951 nearly 10 per cent of Indian girls under 15 and three-fourths of those 15–19 had been married.[8] In such countries as India, Korea, Formosa, and Turkey, practically no women 20—24 are single. It is obvious that, other things equal, the younger the age at marriage, the higher the ultimate fertility, especially since a woman's reproductive capacity is apparently greatest in her late teens and early twenties.

4. With an emphasis on kin solidarity *the compulsion to marry is often quite strong.* Especially with patrilocal residence arrangements, the daughter may be viewed as a potential liability to her family of orientation, to be satisfactorily married at all costs. From the standpoint of the groom's family, a marriage represents not only an alliance with another strong family line but also an essential means of expanding one's own agnatic line. The necessity of getting one's children married may indeed be viewed as a religious and moral obligation. As a consequence, fewer persons go through life without marrying than in the case of the industrial nations. In fact, in India in 1891, a higher proportion of women aged 20–24 had been married (97.3 per cent) than were ever married by any age in Western countries. In Denmark in 1787, for example, only 91 per cent of the women aged 45–49 had ever been married; and in France in 1881 only 87 per cent of the women of this age had ever been wed.

5. *The young wife is motivated to have offspring as early as possible and in considerable number.* Given the joint family and the prevailing rule of patrilocal residence, the bride is a stranger among her husband's relatives. Because of her newness and because of her youth, she is often assigned a low position in the restricted hierarchy of women. She has little she can call her own until a child is born. The birth of a son proves her contribution to her husband's line and thus begins her rise to a higher position within the domestic circle. Offspring also give her something to lavish her affection on, something on the basis of which she can stand up for herself. In cultures where the father's bond with the child is a strong one, the birth of offspring gives the wife extra standing in his eyes; and in cultures where divorce is easily possible for the male, as in most Muslim countries, the wife views offspring as a means of holding her husband. Under such circumstances it is not strange that a young married woman has little incentive to avoid childbirth.

6. *The man is strongly motivated to demand offspring.* The structure of the joint family ordinarily rewards not only the mother's but also the father's reproduction. Often the children are viewed as belonging to him and his family, and the sons as perpetuating his family line. More tangibly, numerous children help to strengthen the patrilineally organized composite family by the sheer weight of numbers. Insofar as this family remains a viable economic and social unit, it gains economic and political strength by having an abundance of youthful members. Young adults can thus provide security for their old age even when few other means are available, and they are encouraged to do so by their elders.

The male's motivation is seen further in what may be called "sociological cures" for sterility. A barren wife not only suffers stigma, but she may be divorced to make room for a new and presumably more fertile wife. A woman who bears only daughters may suffer the same fate. In addition, in some agrarian cultures at least, the wife's

[8]See K. Davis, "Fertility Control and the Demographic Transition in India" in Milbank Memorial Fund, *The Interrelations of Demographic, Economic, and Social Problems in Selected Underdeveloped Areas* (New York: Milbank Fund, 1954), pp. 85-86.

barrenness may be a just cause for the acquisition of a concubine or a second wife or for the adoption of children of her husband's relatives.

The Segregation of Male and Female Roles

So far we have traced some of the effects of subordinating the nuclear family to wider kinship groups. An additional influence on fertility is the tendency of stable agrarian societies to segregate sharply the roles of men and women. This tendency is often connected with the dependent status of the nuclear family in the joint household, because when several related men and several women dwell together, strong avoidance rules are required to reduce the possibility of prohibited sexual contact and sexual rivalry. But the segregation of male and female roles is found in agrarian societies with or without joint household arrangements, and thus may be viewed as a somewhat independent factor in high fertility.

The institutional restriction of the feminine sphere may reach an extreme degree—as in the practice of purdah in Muslim and to some extent in Hindu culture, and in the seclusion of females in agrarian Latin cultures. The effect of such limitation is to confine women largely to the household and to identify them with reproduction, so that their lives revolve around home and children. Female education is regarded as unnecessary if not actually immoral. Women, therefore, have little knowledge, sophistication, or independence. They cannot conceive of a glamor role or a career role which would compete with the childbearing role. They cannot complain that children prevent their getting outside the home, because outside activities are excluded anyway.

With the segregation of roles, the gulf between the man's and the woman's world becomes so wide that communication between husband and wife is reduced to a minimum — particularly with reference to sexual topics, for the woman is supposed to have no knowledge or initiative in such matters. Curiously, husband and wife in many cases may never discuss the one thing that presumably represents their special bond, sex and reproduction. Toward this aspect of life the woman has mainly a nonrational approach—religious, superstitious, and incurious. The husband views reproduction as his prerogative, something taken for granted and involving simple compliance on the wife's part.[7]

A further consequence of feminine seclusion is that, when economic development first begins, women do not proportionately enter the industrial and commercial labor market. As a result the cities in many underdeveloped areas (notably in Asia) are heavily masculine.[8] The occupations that Westerners now regard as chiefly feminine — nursing, teaching, stenography, domestic service, retail selling — are generally staffed by men. Entry into such occupations would take women out of the home and give them a sense of conflict between pregnancy and economic gain. Also it would take them to towns and cities, where rearing children is more difficult. The exclusion of women from the labor market therefore continues for them the conditions favorable to high fertility even after considerable economic development has occurred.

Agrarian Society and the Family

The features of family organization barely sketched above are well adapted to a peasant mode of existence. In traditional agriculture the main instrument of production, apart from land, is human labor. To

[7] J. M. Stycos and Reuben Hill have particularly emphasized the lack of communication between husband and wife as a factor in high fertility. "Prospects of Birth Control in Puerto Rico," *Annals of the American Academy of Political and Social Science*, Vol. 285 (Jan. 1953), pp. 140-142. Also, "Cultural Checks on Birth Control Use in Puerto Rico" in Milbank, *op. cit.*, p. 61.

[8] See Eunice Cooper, "Urbanization in Malaya," *Population Studies*, Vol. 5 (Nov. 1951), pp. 125-126; K. Davis, *Population of India and Pakistan* (Princeton: Princeton University Press, 1951), pp. 139-141. The cities of 500,000 or more in India in 1931 had 175 males for every 100 females.

learn any skill involved does not require formal education but merely observation and practice. Children can thus start producing at an early age. Women can work in the fields and in the household handicrafts without much hindrance from constant childbearing. Furthermore, the type of agriculture in which most of the product is consumed at home rather than sold, in which hand labor substitutes for capital, and in which the level of living is consequently extremely low — this is the type in which the means of transportation and communication are scant, and in which consequently the rural village is extremely isolated. The state, in such circumstances, tends to be a distant mechanism scarcely less rapacious and unpredictable than the marauding thieves from which it supposedly protects the village. The village must therefore protect itself as best it can. Its means of social control must be strong, and thus family controls and the authority of the elders can be easily enforced. Without much geographical or social mobility, kinship can serve as a principal basis of social position. The division of labor can be simple, resting heavily on the ascription of status on the basis of kinship, caste, age, and sex. With mortality high from disease, occasional famine, disaster, and war, the constant struggle is to maintain the population. Children strengthen and continue both the family and the village, and the institutional mechanisms favoring their appearance are strongly rooted.

The whole economic and family context represents an intricate and tightly integrated complex which can survive an amazing number of vicissitudes and last for an amazing length of time. Favorable conditions are responded to by an irrepressible expansion of numbers; unfavorable conditions are met by a remarkable power of survival and recuperation. As a consequence the stable agrarian mode of life has achieved a wide distribution over the world and still includes over half of humanity. It has in recent times encountered a force strong enough to liquidate it — the impact of urban-industrial civilization. But the corrosive power of this impact is not always manifest. Sometimes it affects the stable agrarian society, not as an unfavorable condition, but as a favorable one. If the underdeveloped area continues to remain agricultural, its participation in the world economy being that of a supplier of raw materials; if security is guaranteed by a colonial government or by world peace; and if mortality is reduced by the impact of modern medical science and public health — if these things happen, as they often have, the effect is to maintain those parts of the social structure most favorable to a high birth rate. The agrarian society therefore expands; it may even send millions of people overseas while its home population is growing rapidly. Eventually, however, the expansion runs into problems of congestion. Conditions either must become worse and the expansion cease, or industrialism must destroy the agrarian institutional complex and thus substitute a new economic and social order which no longer responds to economic growth by an automatic, reflex increase of population.

Religious and Ethical Values

Little has been said thus far about the role of religious values in maintaining a high birth rate. The omission is deliberate, for it seems more reliable to reason in terms of social organization than in terms of avowed values. Above all, care must be exercised in accepting sacred literature or priestly doctrine as evidence of a society's actual values. Motivation is always motivation within a situation. Without an awareness of the circumstances in which people are placed, we can say little or nothing about their values. The latter at best tend to be vague and protean, furnishing the observer with a skimpy basis for predicting behavior.

However, it is worth noting that the religious paraphernalia of agrarian societies is generally in consonance with the institu-

tions producing a high fertility. The desire for sons in patrilineal societies — whether the religion be Muslim, Hindu, or Buddhist — is reinforced by supernatural beliefs and ritualistic practices. The authority of the elders is strengthened by the tendency to regard them as somewhat sacred, as being near the other world. The segregated role of the woman is ritualistically defined, so that its violation becomes a religious as well as a moral offense; and the wife's subordination to the husband may be expressed by worship of him and his lineal ancestors. All told, despite the diversity found in different cultures, the value system seemingly serves to bolster the institutional arrangements already described.

Balancing Factors

Our intention has not been to imply that every feature of agrarian social structure favors fertility. On the contrary, any social order has functions other than reproduction which its members must perform, and some of these are both partly antithetical to reproduction and equally as important for societal survival. It follows that no society is so organized as to get from its women anything near the maximum childbearing of which they are biologically capable. Some of the mechanisms that dampen fertility are the prejudice against widow remarriage (Hindu), the taboo on intercourse after childbirth (many cultures), easy divorce (Muslim), monogamy, an insistence on legitimacy, restraints on medical knowledge and practice with reference to pregnancy and parturition, and the prejudice against procreation after grandchildren have already appeared.

However, our purpose here has been merely to consider some of the widespread institutional patterns favoring reproduction, particularly in the massive agrarian societies that are archaic rather than strictly primitive. These societies respond to urban-industrial penetration usually by maintaining much of their social and familial organization. Truly primitive peoples, on the other hand, experience more of a shock on direct contact with advanced peoples. In this case both a rise in mortality and a decline in fertility often occur, making survival extremely difficult. Primitive societies which survive such a shock sometimes have their institutional organization so altered that, when mortality is reduced, the disfunctionally high fertility may not persist long. It seems likely, for example, that the societies formed from slave populations in the West Indies will achieve a modern demographic balance sooner than those formed by Asian peasants (e.g. in Formosa). At first it might be thought that family disorganization, as observed currently in the British West Indies, would be conducive to high fertility in virtue of the lack of institutional restraint on sexual relations. But no society can avoid placing responsibility on somebody to take care of the child — if not the father, then either the woman who bears the child or whose daughter does so. The institutional system, being disorganized, puts no particular restraint upon the woman's protecting herself by reducing childbearing.[9]

All told, the big agrarian societies appear to be the ones where the institutional supports to functionless reproduction are likely to be strongest, to persist longest, and to cause the greatest demographic imbalances. It is of great sociological interest to study the process of change by which this functionless fertility is gradually eliminated through alterations in the reproductive institutions.

[9]See Judith Blake, "Family Instability and Reproductive Behavior in Jamica," to be published soon in the proceedings of the 1954 conference of the Milbank Memorial Fund.

THE EVOLUTIONARY PROBLEM OF GENETIC DISEASE

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ONE OF THE MOST important and interesting phenomena in the field of human genetics is the persistence of genetic disease, despite the fact that affected individuals are generally severely hindered in survival and fertility. The explanation of this phenomenon must lie with the concept of the balance of evolutionary forces affecting the frequency of hereditary disease. The purpose of this article is to examine the consequences of upsetting this balance through the introduction of effective therapies for genetic disease (effective referring to the increase in survival and fertility of affected individuals). Since significant headway has already been made in the treatment of hereditary disease (e.g., diabetes mellitus and acholoric jaundice), the problem posed for examination is not entirely within the realm of speculation.

The major evolutionary factor involved in this phenomenon of the persistence of genetic diseases is that of selection pressure, which is the population geneticist's method of comparing the relative capacities of alternative types to leave viable offspring. For example, we speak of selection (selection pressure is selection quantified) against the hemophiliac, since he leaves less offspring on the average than the non-hemophiliac. We could just as accurately speak of selection in favor of the non-hemophiliac, since he leaves *more* offspring than the hemophiliac, which illustrates the simultaneous, positive and negative aspects of selection. However, in a eugenic sense, we *do* speak of selection as being *either* positive or negative, which in this case refers to the mode of implementation of an artificial selection program—positive selection referring to the increase of reproduction of the desired type, and negative selection to the decrease in reproduction of the undesired type.

We can see then, that an effective therapy for a genetic disease either diminishes or eliminates the selection pressure acting against it. Prior to the diminishing of the selection pressure, some opposing evolutionary force, such as mutation, must have been operating to keep the disease reappearing in the population (balance of evolutionary forces). Now, with this force (e.g., mutation) unopposed, we can expect a general increase in the frequency of the disease. In fact, under such conditions we can conceive of the spread of a genetic disease through an entire population.

The first question that comes to mind with respect to this phenomenon is that of the magnitude and rate of increase of such treatable hereditary diseases. The rate and/or extent of the change in the frequency of an hereditary disease, after an effective therapy has been found for it, will depend on its frequency and on the evolutionary mechanisms maintaining it in the population. The higher the frequency of a lethal trait, the greater must be the magnitude of the evolutionary force keeping this disease in the population against the eliminating force of selection. When the selection pressure is diminished through the intervention of medicine, then the frequency of the hereditary "disease" will increase at a correspondingly rapid rate. Furthermore, if, for example, mutation is the evolutionary force involved, the rate of change will in general be very slow, while the extent of change might be 100

per cent establishment of the hereditary disease. On the other hand, if compensation (families producing affected offspring have more children on the average than families having only normal offspring) is the evolutionary factor concerned, then it is even conceivable that there would be no increase in the frequency of the hereditary disease following the introduction of the effective therapy. As was mentioned, population geneticists have been highly interested in these general questions. They have thoroughly explored the theoretical aspects of the evolutionary mechanisms involved in lethal or sublethal (hereditary disease) systems and they have made a good beginning in estimating the frequencies of various hereditary diseases. But they have barely scratched the surface in determining which evolutionary force or forces are involved in any specific disease. Although determining such evolutionary forces is empirically the most important for our purposes, we can still obtain a general picture of the magnitude of the problem through our theoretical knowledge of evolutionary mechanisms and what we know of the frequency of hereditary diseases.

For simplicity, we will consider the change in the frequency of a more or less hypothetical hereditary disease under the different evolutionary mechanisms possible and under the assumption that selection pressure has been removed from the disease. It will be best here to assume a simple recessive lethal disease (due to homozygosis for a single recessive gene and where none of the affected individuals reproduce) with a maximal frequency (.0025), since that will allow us to examine its change under all possible systems and will also give us the situation at its worst. The frequency (.0025) of the disease chosen here is one estimate given for hereditary sickle cell anemia in the American Negro population.

There are four general evolutionary systems which could maintain a lethal recessive in a population against the pressure of adverse selection, and these will be considered in the following order: (1) mutation, (2) selection in favor of the heterozygote, (3) gametic selection, and (4) compensation.

1. If the rate of *mutation* is the only force maintaining a recessive lethal in a population at a constant frequency, then the magnitude of the mutation rate is related to the frequency of the disease in the following simple manner: Mutation rate from normal gene to lethal recessive gene is equal to the frequency of the disease (homozygous recessive). This relationship holds very closely even under conditions of inbreeding, at least for the magnitude of inbreeding we can conceive of as occurring in man. So, for our example, where the frequency of the disease is .0025, the mutation rate would also be .0025, which means that 1 in 400 gametes (sperm and ova) will carry a mutation for the disease-producing gene. Although this may appear to be an inconceivably high mutation rate, it should be pointed out that comparable mutation rates have already been given as estimates for human genes (Goodman and Reed 1952).

Then, if the selection pressure against the disease is completely removed, the frequency of the disease will increase at a rate directly related to the rate of mutation. We need not go into the exact formula for this increase, but we will make a calculation here to see how many generations, or years, it would require under these conditions for the disease to reach serious proportions. A frequency of 10 per cent has been chosen (that is, one in every ten individuals would require treatment for this hereditary condition) as a figure of serious magnitude, and though this choice is arbitrary, it is doubtful if this value would be challenged, at least as a minimal one.

It will be assumed in this estimate that the back-mutation rate is insignificant (mutation from the disease-producing gene to the normal one) which is in accord with the general experience from experimental genetics. Even if a small back-mutation

rate is assumed, it will not alter the results for this calculation appreciably. A back-mutation rate would be of most significance in preventing the complete spread of the disease-producing gene through the population. That is, there would be a point at which the opposing mutation rates would cancel out each others' effects, and no further change in the frequency of the disease would occur.

The time then for the hereditary disease under discussion here to reach a frequency of .10, starting from a value of .0025, and at a mutation rate of .0025, would be approximately 150 generations or about 4000 years. To most people this period is almost certainly too long to be of any concern, particularly in view of the fact that we are considering an extreme situation.

2. In *selection in favor of the heterozygote*, which is the next evolutionary system to be considered, the carriers of a single lethal gene for a particular disease (they do not exhibit the disease themselves) leave more viable offspring on the average than those individuals who carry none. Therefore, an opposing force is set up counter-balancing the selection pressure eliminating the homozygous recessives, and, consequently, the lethal trait is maintained in the population.

For a rare recessive lethal disease, where selection in favor of the heterozygote is the only factor maintaining the gene in the population, the selective pressure in favor of the heterozygote is about equal to the frequency of the gene for the lethal trait.

This means then, that for our example, this selective value will be the square root of .0025 or .05, and when the pressure of selection against the lethal disease is removed, the frequency of the trait will increase at a corresponding rate. Now, although the frequency of the disease will increase at a much faster rate for this case than for the previous one considered (mutation), there will be no possibility here of the disease spreading throughout the entire population. The higher selective value of the heterozygote will prevent this, just as it prevented the elimination of the lethal trait prior to the assumed medical intervention.

In fact, the most reasonable assumption for such cases is that the frequency of the disease will not go beyond 25 per cent. Estimating again the time required for the trait to increase to a frequency of .10—starting from an initial value of .0025 under the above conditions—the period calculated will be approximately 75 generations, or about 2000 years. This is just half the time required for the same change under the previous hypothesis discussed (mutation).

It is interesting to note that, for the case of selection in favor of the heterozygote, by eliminating this selective advantage rather than introducing a therapy for the recessive lethal condition, the evolutionary consequences will be completely reversed. In fact, in the same period of time that we calculated as necessary for the frequency of the disease to reach 10 per cent under the condition of an effective treatment for it, we find that the disease frequency will be reduced to .02 per cent under conditions of equality of selective values for the heterozygote and homozygous dominant. This aspect of the problem is particularly interesting, since Allison (1954) has recently brought forth convincing evidence that this very phenomenon is occurring in the case of sickle cell anemia. His work indicates that selection in favor of the heterozygote is the major factor accounting for the maintenance of the sickling gene in some African populations, and, furthermore, that this selective advantage is due to the greater resistance of the heterozygotes to malarial infection than the normals or homozygotes. With the introduction of mosquito control programs (which in turn control the malarial parasite) into these areas, it is very likely that the selective advantage of the sickling heterozygote will be eliminated and, consequently, the frequency of the sickling gene and also the sickling disease reduced. In fact, as Allison points

out, it is the relative absence of the malarial parasite in America which is probably the major explanation for the lower frequency of the sickling gene in the American Negro population as compared with the African Negro population. In other words, the sickling heterozygotes in America would not have a selective advantage as they do in certain parts of Africa, which incidentally would be a most interesting and important possibility to check.

3. The next evolutionary system to be considered is that of *gametic selection*. Here one type of gamete has an advantage over the other or others in the process of fertilization (in our hypothetical case, the gamete containing the disease-effecting gene), and this behavior opposes the eliminating pressure of selection on the affected individuals, thereby maintaining the lethal trait in the population. For the example under consideration, a 5 per cent advantage of the lethal gene at the gametic stage would suffice to offset the lethal effects of this gene in the homozygous recessive genotype or the zygotic stage.

Then if the selection pressure against affected individuals is removed through the introduction of an effective therapy, the frequency of the disease would reach 10 per cent in about 45 generations, or around 1250 years. Furthermore, under these conditions the hereditary disease could conceivably spread throughout the entire population. Although specific examples of gametic selection are not known in man and indeed would be difficult to demonstrate conclusively, it is very likely that the surplus of males at birth are a result of gametic selection in favor of the Y-bearing sperm; this advantage being counterbalanced by the excessive mortality of the males in the zygotic stage.

4. Finally we come to the fourth and last evolutionary system under consideration: *compensation*, where families producing affected offspring tend to have more children on the average than other families. Assuming an average family size of 2.5 (Osborn 1951), this would amount to approximately .5 offspring (average family size 3.0) more on the average per mating producing affected offspring than for matings not producing affected offspring. This will counteract the pressure of selection against affected individuals, thereby leading to the maintenance of the hereditary disease in the population. With selection pressure against affected individuals removed, as we are hypothesizing in this paper, the frequency of the disease would increase very rapidly, assuming that the compensating mechanism remained constant. In fact, it would take less than 20 generations, or less than 500 years, for the frequency of the disease to reach 10 per cent. However, it seems highly doubtful, at least to this writer, that this mechanism would remain, once the debilitating or lethal nature of the hereditary disease had been eliminated. This assumes, of course, that the compensating force is psychological in origin or, to put it more strongly, under willful control. The possibility must certainly be admitted, however, that this mechanism might *not* be willfully controlled.

It is of interest to note in concluding the discussion in this section that compensation has been considered as an important evolutionary factor in the persistence of more than one genetic disease (Lewontin 1953).

It can be seen, then, that the potential magnitude of this problem—the increase in the frequency of a hereditary disease once an effective therapy has been found for it—can range all the way from no increase in the incidence of the disease to a condition under which the disease could reach serious proportions in less than 20 generations. Some may argue that we are dealing here with a very extreme case, and therefore the potential seriousness of the problem is unduly magnified. It is certainly true, as was stated earlier, that we have chosen an extreme case for consideration, but it appears that for medical problems of such sig-

nificance, the only reasonable approach is to do just this. Certainly, in buying insurance, the average man will insure against the maximum hazards.

Furthermore, we must remember here that our calculations dealt only with changes in one disease at a time, when in actuality this general process will be taking place simultaneously for several such hereditary traits. This of course would greatly augment the magnitude of the problem in that there would be many more people requiring treatment for one disorder or another and some individuals would require therapy for more than one.

It seems clear, then, that the problem for any one case may be of serious proportions, depending of course into which of the previously discussed categories, if any, a particular hereditary disease falls. The first order of inquiry in any situation, then, is clearly the nature of the evolutionary mechanism maintaining the disease in the population. This information is necessary in order to determine the expected magnitude of the problem, which factor in turn will be the foundation for any discussion of what should and can be done about it.

The study of these evolutionary mechanisms has been, and still is, of great interest to the population geneticist. But unfortunately, it is not simple to discover which mechanism is responsible for the maintenance of a particular genetic disease in a population. For example, geneticists have spent considerable effort investigating this very problem in the case of Cooley's anemia, a lethal hereditary disease found in relatively high frequency among Mediterranean people. Consistently, there have resulted as many hypotheses as to the nature of the evolutionary mechanism involved as there have been investigations. Of course, it is quite possible that a combination of factors would be responsible for the preservation of a lethal disease in a population, and we must be prepared for such a possibility.

However, it is doubtful if this is the major factor accounting for the lack of success in arriving at a definitive answer for a disease like Cooley's anemia. The real trouble appears to lie in the fact that, in order to distinguish with any reasonable degree of probability between the different possible hypotheses, very large numbers of individuals must be observed, and thus far this has been beyond the scope of any one investigation. In fact, for some of the rarer hereditary diseases, it is quite likely that surveys of nationwide scope would have to be conducted to arrive at statistically sound conclusions. However, despite this difficulty and others which we shall not go into at this time, sufficiently extensive studies seem possible in most cases which will permit definitive answers on this high important question.

The potential increase in the frequency of a treatable genetic disease has been discussed as an undesirable consequence of the phenomenon under discussion. The main argument for this view is the increasing medical burden that such a process would bring to bear on a society. There is also the argument that a society largely dependent on medical therapies for its maintenance would not be a very secure one. However, it should be noted that other viewpoints on this problem are conceivable. For example, in the case of a recessive lethal where selection in favor of the heterozygote is responsible for maintaining the gene in the population, the introduction of an effective therapy for the disease would not only lead to an increase in its frequency but would also increase the frequency of the favorable heterozygote. This would result in an increase in the adaptive value of the population, which essentially means an increase in its reproductive efficiency. However, whether this effect would counterbalance the medical, social, and financial problems arising from the increase in the incidence of the disease is certainly questionable. Furthermore, this is a statistical outlook attempting to evaluate the overall effect of this process on the

population and does not take account of the many individual hardships created by it.

Finally, the question of future action on this important question arises. There are only two methods we know of at present to counteract such increases in treatable hereditary disease, and one, the restriction of medical therapy and/or research, would probably be universally unacceptable. The other method, is, of course, a eugenics program which would require a great deal of public education before it would become widely acceptable. However, for some cases it would appear that a eugenics plan could be made workable. For example, where selection in favor of the heterozygote is the major evolutionary force involved in the maintenance of the lethal gene, reduction of the heterozygote's fertility by less than one offspring per family would most likely more than suffice for all situations. It seems conceivable that a voluntary reduction in reproductivity of this order of magnitude could be achieved.

However, such decisions as will be made on these matters will depend largely on which evolutionary mechanisms are involved in any particular case, since only then will we have some idea of the time factors involved. Therefore, it seems highly desirable to set up extensive investigations capable of answering the question of which evolutionary mechanisms are involved in maintaining any particular hereditary disease in the population. It is only with such decisive information that we will be able to evaluate the nature of this hereditary dilemma and to consider fully the frustrating and interesting questions which it poses.

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EDUCATION FOR PERSONAL AND FAMILY LIVING*

FREDERICK OSBORN

UNTIL RECENTLY, personal and family living was not considered the community's business. A man could lay down his own rules, taking into account the admonitions of the church. He could kiss his wife in the morning and be pleasant to the children at a leisurely breakfast, or he could leave the whole house in an uproar as he ran for the 8:05 train; the choice was his and it was no one else's business.

Now rather suddenly, we've found out that personal and family behavior is the business of the whole community, because ultimately it reacts on the whole life of the community. Ill-adjusted personal and family lives provide the basis for the mistakes in social behavior which help fill our jails, crowd the divorce courts, and wreck the lives of so many of our children. So we have come to the very natural conclusion that we should do something about it, and we have lately been making quite an effort in that direction. But, in general, the methods we have used in the past to control man's behavior in his social relations don't seem to work as well in this field of his personal life. We tried to regulate his personal life by prohibiting the sale of liquor. It didn't work. It is a much more difficult job to make people stop nagging their wives, neglecting their children and making themselves and others generally miserable.

The fact is that the basic elements of personal and family living are learned in the home and at a very early age. This is generally recognized, and so we make an effort to educate parents on how to educate their children. But this effort comes pretty late. By the time they are parents the personality difficulties which they acquired as children stand in their way. We have got to find a new approach.

There is a new approach to this problem of education for personal and family living. It is quite untried and may be disturbing to some people because of its novelty. I would like to explore it with you. First, let us look at some of the accepted findings on which the new approach is based.

Parents who are normal thoughtful people, responsible, sensitive in their relations to others, and who have conceived their children with a full sense of responsibility for their care, turn out better children on the whole than do parents who are irresponsible, lacking in kindness to others, unstable in their affections and purposes. This is a matter of general observation. It is also the finding of the many studies which have been made in this field. If all children were brought up in homes where affection and kindness, steady and sensible authority and intelligent interest were the general rule, there would be little juvenile delinquency, and personal and family living would be immeasurably improved, im-

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mediately and for each succeeding generation. Obviously, there are many such homes today; perhaps a majority would fulfil most of these requirements. But there are many homes which obviously do not measure up to these standards. The community suffers, now and in the next generation.

Another set of facts which should influence our thinking lies in the present trend of births. In the old days children came when people were married, regardless of whether they were wanted or not. Size of family was more a matter of luck or of biological possibilities than of anything else. In England, women married at the middle of the nineteenth century bore, on the average, six or more children. Today in the United States, in Sweden, and probably in most of the countries of western Europe, a large proportion of, but certainly not all, married couples consciously limit the size of their families. In the United States, as in England, family limitation started in the upper economic classes and worked down. This has made for so-called class differentials in births, the upper income groups having fewer children than the lower income groups. But recently a new and interesting trend seems to be developing. When we study only those couples whose childbearing is effiectively planned, we find that couples with the larger incomes have more children than do the couples with smaller incomes. This is a reversal of all previous trends. All recent studies, when limited to couples who plan their families effectively, indicate such a trend; none that I know of show any different result. Unfortunately, few of these studies relate size of family to the quality of the parents but only to their incomes, though some recent studies of college graduates indicate that the men more highly regarded by their classmates as good citizens have more children than their less highly regarded classmates.

These indications have exciting implications. If, under effective family planning, income status reverses the old differentials, perhaps other social and even psychological factors can also influence the size of planned families. Perhaps the community itself can create and develop conditions which will result in a larger proportion of the community's children being born in the homes where they will get the most affectionate and responsible care. Then we would have an alternative to the almost impossible task of teaching improper parents to do a better job for their children. If a larger proportion of children were born in homes which fulfill generally accepted requirements for a sound environment for child development, and a smaller proportion of children were born in homes which do not fulfill such requirements, we would be approaching nearer the ideal of having all our children well educated for personal and family living. The fact that people have now accepted the idea of family planning, even though they don't yet all practice it, gives such a proposal a reality it did not previously have.

As yet we have no social experiments or scientific studies which offer definite proof that such a plan would work, but it is a reasonable assumption that it would. It is a matter of common observation that people do not live entirely to themselves. They respond to the physical conditions of their environment. They are influenced, consciously or unconsciously, by what their friends think, by the attitudes of their doctor, their nurse, or of the social worker who pays them visits. These influences are indirect; people will still be making up their own minds as to how many children they are going to have. But perhaps we could help them make up their minds by introducing social and psychological pressures of a sort to get more children born in the home environments best suited to child development.

Most community facilities, by their absence or by their availability, come under the head of social pressures. The availability of good schools is one of the more important factors entering into decisions as

to size of family. Housing facilities appropriate to a large family at not too high a cost may also be important. Nearby and attractive playground facilities, good and not too expensive medical care, day nurseries, the availability of baby sitters—all the facilities which relieve the young mother of the monotony and extreme weight of caring for several children at once must be influences of importance in decisions as to whether to have another child. These and many other things which will suggest themselves are already being done for the purpose of improving the health and well-being both of children and of their hard-pressed parents. They will get even greater support when we also think of them as means to encourage responsible parents to have larger families.

It is possible that, when the community itself gives more thought to its children and the encouragement of their parents, the less responsible parents will think more about their children and about restricting their number. The less responsible parents may also be affected by other measures. They can be made to contribute more to their children's support in case of divorce. They can be held to stricter accounting for their children's attendance and behavior at school, for their proper nutrition, for their medical care. It does not seem reasonable that irresponsible parents should have nothing to pay at free medical clinics while careful parents have to provide their own medical services.

Psychological measures may be even more important. Decisions as to whether to have another child are inevitably influenced by what the neighbors think, and by the attitude, felt if not actually expressed, of the advisors with whom the parents come in contact in the ordinary course of their lives. Their doctor may warn them of dangers of having another child, or, on the other hand, he may admire their large family, their health, their good bringing up. The nurse can encourage them in similar ways, or she can point out that the number of children they already have is straining their resources to the limit. The minister or priest, more perhaps than any other person, should be concerned that children should only be conceived with a full acceptance of the responsibilities of parenthood and should encourage large families in homes which follow the teachings of good personal and family living.

Finally, the attitude of the community as a whole will be perhaps the most important factor of all. There have been communities, and there may still be some today, where couples who had more than two children were laughed at and made the objects of sympathy for their carelessness or incompetence. There are other communities where, especially since the war, it is the fashion to have families of three or four. It would be hard to believe that these community attitudes do not exercise a very real influence on people's decisions to size of family.

The consideration of community attitudes emphasizes what is perhaps the major difficulty in developing a practical program for changing the proportion of children born in different kinds of families. We are not trying to increase the aggregate number of children born, nor are we trying to have fewer children born. We are attempting the much more difficult job of creating conditions such that children will be born in larger proportion in homes which will give them the most affectionate care. It is not enough for a community to provide the same facilities for all its children. It must seek to provide conditions which will make a special appeal to the most responsible parents. This is difficult but perhaps not so difficult as it might seem at first glance. We are not considering any form of coercion. Nor do we need to get any exact results. Nature does not work that way, nor need we try to. It will be enough if on the whole we reinforce and give direction to the trend which is already in a small way beginning to show itself. Every advance in the proportion of children

born into the homes where they will best develop will be a gain, and we need not worry too much about the exceptions. But even taking all these things into account, it will not be easy to develop a public attitude which will accept variations in size of family. People like simple ideas. They enlist in movements for everyone to have fewer children. Or, as in France they join "La Ligue de Familles Nombreuses." It would be harder to get people interested in a more complicated idea, making size of family appropriate to the child environment offered by each particular home.

The idea that some couples should have greater freedom to have large families and other couples greater freedom to have small families can be misunderstood to imply the kind of personal judgment people do not like to make. But we are proposing only that every couple should pass their own considered judgment on what they themselves want, in the light of their own values. We are proposing that every married couple should have the size family they would want to have if they had a full understanding of their responsibility to their children, of the sacrifices which will be expected of them, of the kind of patient and thoughtful bringing up they will have to give their children if they are going to get happiness out of them. We are proposing that the community should make every effort to give all married couples an early understanding of the values and responsibilities which accompany parenthood.

We are proposing that the atmosphere and environment of our communities be such that children would be conceived only by couples willing and able to undertake these responsibilities; that size of family should be determined by the parents after fully weighing their desire for children, and the sacrifices which they will have to make in bringing them up, against other things they want but will have to give up if they have children or many children.

We are proposing that all our communities should be so developed that the facilities which make for the better development of its children and for easing the strain on young parents should be available to everyone, while the pattern of the rational planning of family size is earnestly encouraged. To some people the rational planning of births may mean birth-control clinics. But to many others it will mean simply a greater sense of responsibility toward getting and rearing children. We should remember that when this responsibility is well recognized the means for planning or limiting size of family may be found in many different forms. In Ireland for instance, where ever since the great famine the necessity for limiting the size of family has been universally recognized, the means adopted has been that of late marriage. In England, when the birth rate dropped suddenly in the latter part of the 19th century after the Bradley-Besant trials, it was not because new means of contraception were suddenly understood and used but because many people for the first time realized that it was proper and right to limit the size of their families to those children they could care for in decency. Every time there has been a rapid fall in birth rates, whether in Japan, or in Russia, in Catholic countries or Protestant, it has seemed to be caused primarily by the adoption of the culture pattern of family limitation, the particular means used to restrict the number of children born being secondary. When people find themselves free and responsible in regard to the number of their children, they seem to seek a reasonable solution, whether by the means of continence, late marriage, contraception or other means. This needs to be pointed out because it should be perfectly clear that the proposal for a better distribution of births does not involve approving or disapproving any particular means of fitting size of family to the home environment. There are moral grounds for approving or disapproving one or another of the means. But the purpose, the aim, a better distribution of births, has almost universal moral support, from that

of the Pope in some of his most recent pronouncements, to that of the Protestant clergy and of contemporary moralists. Only a few isolated sects still believe that men should be fruitful and multiply regardless of the consequences to themselves or to the community.

Of course, there is always the possibility that with advance in medical science means will be found for extending the periods of women's infertility or of producing an easily reversible form of sterility in either man or woman. This would make our proposal even easier to carry out, though it might require a special effort on the part of the community to encourage the birth of enough children to provide for replacement. But such a discovery may be some time off. We can cross that bridge when we come to it.

The first and perhaps the most difficult step in getting this proposal under way is to get the idea understood for what it really is: the attempt to develop a community environment in which, by an unconscious and wholly voluntary process, a larger proportion of children will tend to be born in the homes most appropriate to child development. Along with this understanding must go a recognition that there is no standard size of family, no "ideal" size, except in relation to a particular couple. How many children a couple should have is a matter of their own interests and preferences, just as is their choice of profession. The couple with a large family deserves no more approval or disapproval from the community than does the couple with a small family, so long as the decision as to size has been made with a sense of responsibility. Once this apparently hard-to-understand point of view is accepted, the practical applications become clearer and easier. Actually, there should be little difficulty in getting acceptance for most of the things which would be required of the community. They are all things which are already on the community conscience for quite other reasons. Every community is anxious to do the right thing by its children, with respect to both the atmosphere and the facilities of the community. But if the community understands the larger results, the larger meaning, of its efforts, they will be better directed and more effective.

Summary

Education for personal and family living can be most advanced by working on it at the early ages. There is little likelihood that we can give young children such an education unless it is done in their own homes by their own parents. The very best way to give it to them is to have them born in the homes where they will get it. It is the proper business of the whole community to see to it that the community environment tends to get them born in just such homes. We have already noted that there are beginning indications of an improved distribution of births among couples all of whom practice family limitation effectively. Surely civilized man should have the wit to take advantage of this trend and develop it in an even more favorable direction.

We do not know yet whether or how far such a development can take us toward raising the genetic qualities of man from one generation to another. Scientific research on this problem is urgently needed. It would be hard to believe that the changes in birth distributions here proposed would tend to the deterioration of the race. In any event, the improvement in the social inheritance which would certainly result justifies a great effort to bring about such a change.

The rewards can be enormous. We are entering the age of the rational control of parenthood. Like all great advances it has its dangers as well as its opportunities. If we can avoid its dangers and take advantage of its opportunities, our civilization can be rapidly advanced. No other purpose offers a greater challenge to our communities or makes a greater call on our obligation to future generations.

HEREDITY COUNSELING
Eugenic Aspects of the Premarital Consultation

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The emphasis in medicine is rapidly extending from care to prevention. Both the public and the medical profession have come to accept the view that the function of the doctor is not merely to restore health but also to conserve it, not merely to remedy illness, but, wherever possible, to forestall it.

An expression of this newer medical attitude is the increasing stress on the value and desirability of a premarital examination and consultation. A medical survey and discussion in preparation for marriage often serves to prevent potential conjugal discord, and makes for a more successful marriage and family life.

"Examination for fitness," once commented Dr. Robert L. Dickinson, a pioneer in marriage education, "has become customary for all occupations save marriage and parenthood. Eventually common sense may be expected to demand a similar preparation before deciding on matters so important to the life of the individual and the race. There should be developed a public opinion in favor of a routine consultation (on major physical difficulties and psychic inhibitions) before the announcement of an engagement, followed by a general and medical examination of both bride and groom a month or so before the wedding date is fixed."

The need for some form of medical examination before marriage has long been recognized. Many states have enacted laws making such examinations compulsory. In most instances, however, the primary aim of these laws has been merely to detect the presence of transmissible venereal disease. In the United States, for instance, forty states now require that an applicant for a marriage license present a medical certificate declaring that he or she is "free from all venereal disease." In a few states the requirements are somewhat broader and include other transmissible diseases, but in the main the examinations are generally quite limited in scope, and do not deal with the wider aspects of genetics and eugenics.

Many individuals considering marriage come to the physician for a number of reasons. Mostly they come to obtain the required examination and blood tests, but many of them also seek general information about interpersonal relations in marriage, about sexual anatomy and physiology, about sex techniques and family planning. "Tell us," they may say, "what we ought to know about marriage and family life." The function of the doctor, then, is to provide basic information and whatever guidance the individuals or couple may need to help them make a stable marital relationship.

Some young people, however, come before marriage with specific problems, with questions about the advisability of a particular marriage or about their chances to beget healthy offspring. Usually these questions center around such social or emotional problems as economic difficulties, parental disapproval, differences in age, culture, religion. At times, though, they relate to physical disabilities or genetic traits. One or the other of the couple may be uneasy about some familial mental or physical defect, and they become fearful about the possibility of transmitting such a defect to their children.

In our marriage consultation services at the Community Church and at the Margaret Sanger Bureau we have seen many such "eugenic problem" cases during the past quarter of a century. Among the genetic problems for which premarital or preconceptional counsel is sought are family histories of mental disease or deficiency, epilepsy, diabetes, cancer, consanguinity, and, occasionally, some of the rarer hereditary diseases.

Aware of the responsibilities which parenthood entails and of the tragic consequences of inherited physical or mental disorders, young people are today more likely to seek guidance on eugenic grounds. Often enough, it is true, their fears are unwarranted and based on an inadequate understanding of human heredity, but at times the history may be serious enough to cast doubts upon the advisability of a marriage or of reproduction. The following two cases illustrate both these points:

Miss A was an attractive young woman, twenty-seven years of age, who repeatedly refused to marry any of the several men who had courted her. She always explained it on the basis of one or another incompatibility. During the course of the interview, however, it developed that her mother, who had died at a young age, had suffered from epileptiform attacks which Miss A had witnessed on several occasions during her childhood. These episodes disturbed her profoundly. She had a deep fear that the children she might bear would inherit this condition, and had therefore decided to avoid marriage entirely. In this instance, a thorough discussion and study of the family history failed to show an adequate reason for her fears, and eventually she did marry and now has two apparently normal children.

The other case is that a young man who came to our consultation service to discuss the advisability of marrying a girl in whose family there were several cases of mental disorder. The girl's mother had committed suicide at thirty-eight, an older brother had been institutionalized for some two years, while a second brother was also in a sanatorium. Although the young woman herself seemed to be both physically and mentally well, the man was deeply concerned about the chances that some mental disease might be passed on to their children. The fact that there was some history of mental disease in his family clearly added to the genetic hazards in this case.

The premarital consultation can thus play an important role in preventive eugenics. When doubts arise about genetic traits, an objective study and evaluation of the situation either before marriage or before conception may aid young people in their ultimate decisions about marriage or parenthood or, more often, dispel unwarranted anxiety. It is essental, however, that the physician who would undertake to guide young people in the eugenic aspects of their marriage should himself have a thorough understanding of genetics and of the heredity of human disease. Not many physicians are today sufficiently well equipped to give competent genetic advice. It would be well if marriage consultation centers would have attached to their staffs a well-trained geneticist to whom problems in human heredity could be referred. There is also a need for developing special heredity centers to which both the public and the counselor could turn for authoritative information. At present there are less than a dozen such centers in the United States. Their extension throughout the country would be a distinct aid to the marriage counselor and to the people seeking advice, and an important forward step in the development of practical preventive eugenics.

RELATION OF POPULATION CHANGES TO THE DISTRIBUTION OF GENETIC FACTORS

Report on Meeting 23 of the World Population Conference, Rome 1954

Introduction

In opening Meeting 23 of the World Population Conference, Böök pointed out that the most important fact we have to face in relation to all problems of human populations is the tremendous diversity of the individuals who make up these populations. Cultural diversities have long been studied. The more recent studies of genetic diversities are in the field of the rapidly growing sciences of genetics and biology. But man's diversity in regard to his genetic potentialities has such far-reaching consequences that it should not and cannot be left to the consideration of only biologists and geneticists. If there is to be a realistic science of man, individual and group genetic differences cannot be disregarded.

This meeting is concerned with human genetic differences in the larger framework of population genetics and medical genetics. The genetic base underlying individual differences in mental and emotional development is not yet well understood and is the subject of Meeting 25.

The science of population genetics is just coming of age. Its theoretical aspects were developed more than a score of years ago by Haldane, Wright and others. Its experimental work was confined chiefly to drosophila. Objective data on human beings seemed far in the future. But all this has been changed by the use made of the blood groups in the years since the war, by other means of determining genetically determined traits, and by improved methods of measuring consanguinity.

The papers presented to this session reflect this change. Sanghvi measures the genetic relationship of the different castes in India described by Wahlund as the world's largest experimental material for the study of human genetics. Sutter and Tabah describe the breakup of isolates in France: "l'Eclatment des Isolats." Kishimoto, Matsunago, Komatu, and Furuhata describe differential survival in Japan under different types of mating and for various characteristics. Demographers, geneticists, and anthropologists in great numbers are making objective studies on the population genetics of man. As the psychologists follow suit, our understanding of the effects of migration, racial admixtures, and differential mortality and fertility should make rapid and cumulative growth.

In the medical field, human diversity expresses itself in three main directions, namely, in (1) genetic diseases or defects, caused by specific and potent gene mutations; (2) individual gene constellations which constitute a necessary prerequisite for the environmental causation of a *specific* disorder; and (3) individual gene constellations which constitute an important basis of reaction types to be considered in terms of vulnerability or predisposition for disease as well as for health and in terms of individual response to therapeutic measures. The first part of the meeting was concerned with these aspects of medical genetics.

The Prevalence of Genetically Based Disease and Defect

The frequency of genetic disease and defects and of specific genetic morbid predispositions was presented by Tage Kemp, Director of the Institute for Human Genetics in Denmark. The prevalence is

very high and consequently of the utmost importance for medical research and practice. By now there are very few medical research workers who do not accept this fact. On the other hand, most of them think of medical genetics as still representing the rather static picture of the early decades of this century, dealing mostly with frequencies, pedigrees and attempts to fit the data into simple, clear-cut Mendelian schemes. Although such analyses remain a basic framework in this field and, together with conventional twin research, serve the purpose of identifying genetically determined morbid conditions, their results now mark rather the beginning than the end of the inquiry.

At present more than 500 different genetic disorders are known in man. Many of them are extremely rare, and others cause only moderate or light incapacity; but Kemp estimates that 2 to 3 per cent of the European or North American populations are severely incapacitated at any given moment; and Böök believes that in these populations the total morbid risk for severe genetic disorders should be of the magnitude of 5 to 10 per cent.

Most of the prevalence figures now available refer strictly to nothing but clinical syndromes which on statistical evidence have been shown to be genetically determined. It is an open question whether or not these syndromes also constitute genetic entities. Recent investigations in various fields suggest that the diversity in regard to genetic disorders is much greater than hitherto assumed. As long as the correlations between clinical and genetic entities remains dubious, the calculations of gene frequencies and mutation rates will also be questionable.

In countries which already have achieved a relatively high standard of living, genetic disorders probably constitute the greatest medical problem of our time, and some of these disorders are on the increase. Among other populations the situation may be quite different. For example, in certain South American or Asian countries where the life expectancy is low, where neither infectious diseases nor nutritional deficiencies are under control, and a substantial part of the population is suffering from chronic starvation, genetic disorders must be of secondary importance in regard to public health. Here the measures should be, in order of significance: (1) birth control, (2) control of infectious diseases and nutritional deficiencies, and (3) control of genetic disorders.

But in European and North American populations genetic disorders have a high prevalence and constitute a major cause of human disease and maladaptation. Consequently they should be a primary concern of public health authorities and medical research workers.

It has become increasingly apparent that each individual is heterozygous for a number of recessive genes with undesirable homozygous effect. The identification of such genes constitutes an enormous task, discussed particularly by Cook.

Among one group of carriers, namely, those who are heterozygous in regard to genes commonly thought of as "incomplete" recessives, Falls and Neel reported that it is now possible to identify the carriers of 29 different disorders. For the future there is the possibility of identifying individual genes or constellation of genes in heterozygous individuals by means of biological stress tests designed to bring out subclinical metabolic deficiencies, by chromatography, electrophoresis and by other refined techniques.

The positive identification of healthy or only slightly deviating carriers of genes which subsequently may cause disease in the carrier himself or only after duplication in his children has a number of consequences. The effect of selection on genetic disorders cannot be fully understood unless the fitness (in terms of effective fertility) of carriers is reasonably well known. The recent discovery that, in certain regions of Africa, heterozygotes of sickle-

cell anemia display a better fitness (immunity to malaria) than the homozygote, deserves serious attention. If such effects should not prove to be rare exceptions, they will render many conventional calculations of gene frequencies or mutation rates worthless.

Dr. J. Bogdan of Rumania took exception to all these conclusions. He held that progressive biology has demonstrated that the development of the individual is determined not by a hypothetical combination of genes but by the conditions of development, that the base of heredity is constituted by the type of metabolism, which in turn can be influenced by the environment, that the so-called pathological heredity determined by a morbid gene is an erroneous conception. The evidence offered for this position, particularly that concerning vegetative hybridization, was held by Lerner and other discussants to run counter to the experience of modern biology. It was felt that the free interchange of ideas among scientists of all countries should help to clear up such misconceptions.

The Mechanism of Gene Frequency Alterations

Changes in gene frequency, both due to chance and to natural selection, are likely to be continually proceeding. The mechanism was discussed by Penrose.

It is reasonable to assume that any hereditary trait which comes under observation is due to a gene whose frequency is not changing very rapidly. Unless a gene were nearly in equilibrium, it would not have survived to be observed. Hence, in order to understand the nature of gene frequency alterations in natural populations, the conditions of genic equilibrium must be studied.

There are three main types of genic equilibrium which can occur. These are:

1. *Neutral equilibrium* (a) with random mating—the Hardy-Weinberg principle—or (b) with deviations from random mating
2. *Stable equilibrium* due to (a) recurrent mutation, or (b) advantage of the heterozygote
3. *Unstable equilibrium* (a) in connection with disadvantage of the heterozygote and (b) in certain types of social selection.

1. *Neutral Equilibrium* (a) The principle discovered in 1908, independently by Hardy and Weinberg, is the classical example of neutral equilibrium. It arises when there is random mating (panmixia) and if no genotype has any selective advantage, expressed either in terms of fecundity or in vitality, over any other genotype. Gene frequency changes which can take place by chance (drift) remain permanent. Within large groups this effect is insignificant, but differences originally produced by lack of homogeneity in small parent populations can remain for long periods. All estimates of gene frequencies made by serologists are based upon the assumption of random mating and absence of natural selection. The fact that good agreement exists between observation and theory in such calculations suggests that the genes concerned are in a state not far from equilibrium.

(b) Deviations from random mating do not disturb the gene frequency provided that all genotypes are equally fit. Thus, neutral equilibrium is compatible with both assortative mating and inbreeding. These processes, so long as they last, increase the proportion of homozygotes at the expense of heterozygotes. The opposite processes of dissortation and outbreeding have the converse effect. There is outbreeding when two previously isolated populations mingle, or in cases of migration, but the gene frequency in the total human population is unaltered. In other respects, deviations from random mating have important consequences. A survey of the effects of consanguinity on stillbirths in France showed a definite positive correlation. Owing to the reduction of inbreeding

in France, as in other European communities, a temporary reduction in stillbirths attributed to lethal recessive genes may be expected.

In such examples as this, genic equilibrium is disturbed and there is selection against the homozygote. The reduction of frequency of the gene concerned is very slow, but it becomes more rapid if there is inbreeding. *Selection against lethal recessives* should therefore be stronger in Japan, and also in India where consanguineous unions are very frequent, than in European countries.

2. *Stable Equilibrium* In this state, if a chance circumstance alters the gene frequency in a population, the original frequency tends to be reestablished. There are two basic types:

(a) Selection against a gene with unfavorable effects can be balanced by the recurrence of fresh mutation. In the typical case, a rare gene with deleterious consequences, diminishing fitness in certain individuals, remains at the same frequency in each generation.

The different gene frequencies of hereditary diseases in different parts of the world may be interpreted as being due to different points of equilibrium between fitness and mutation.

(b) Selection against a gene in homozygous form can be balanced by advantage conferred when it is in heterozygous form. This situation can occur as a consequence of hybrid vigor, sometimes called heterosis. Provided that it is permanent, the advantage of heterozygote need only be very slight in order to preserve equilibrium in random mating. An increase of just over 1 per cent in the fertility of heterozygote above that of normal homozygote will balance a rare recessive lethal gene with 1 per cent gene frequency.

This equilibrium is stable because there would be gradual restitution of the previous state after a chance disturbance of gene frequency. Moreover, after an alteration in fitness of one of the genotypes, provided that the heterozygote still remains the fittest of the three, a new stable frequency is eventually reached. The stability of the process makes it a powerful method of preserving polymorphism in a natural population. This can apply both to genes for segregating traits and to genes producing metrical variations, like stature.

Inbreeding and especially assortative mating can neutralize, or even destroy, the stability of "heterosis" equilibrium: to maintain stability in such cricumstances, the advantage of heterozygote must be correspondingly larger. The observed differentials in fertility connected with intelligence are marked enough to maintain equilibrium even in the presence of the very high degree of assortation for this trait which occurs between husband and wife.

3. *Unstable Equilibrium* (a) The converse of heterosis occurs when the heterozygote is less fit than either homozygote. A system of this kind occurs in connection with antigenic incompatability. It produces unstable equilibrium at a point where the antigen causing incompatibility has gene frequency of 50 per cent because the two homozygotes are equally fit. In the region of this percentage, the gene frequency will only change very slowly though the extermination of a rare antigen, if unbalanced by mutation or heterosis, would be quite rapid. Conversely when an antigen is very common, the instability is shown by its tending to become universal at the expense of its neutral allele.

It is interesting to note that, in European populations, the gene for the D-antigen and that for the A-antigen, which have frequencies of about 59 per cent and 29 per cent, respectively, are near enough to the point of unstable equilibrium, at 50 per cent, not to change very rapidly even under strong selection produced by incompatibility.

Only a very slight advantage in surviving heterozygotes is necessary to produce stable conditions, which would occur, theoretically, at any specified gene frequency.

The search for increased fertility of surviving heterozygotes in the blood groups which would keep the system in equilibrium has not yet been intensively pursued, though some of the papers presented to this meeting provide pointers. Roberts pointed out that more is known about geographical variations in the frequencies of the AB and O blood-group genes in man than is known about the similar conditions of any other plant or animal genes whatsoever. The AB and O groups also confer high selective advantages or disadvantages quite apart from their antigen properties.

Various Factors Which Influence Distribution of Gene Frequencies

The discussants were generally agreed on the following findings as summarized by Stern:

A prolongation of the mean expectation of life is liable to increase the frequency of certain genes in the population because of the increased proportion of older people.

Medical advances often permit survival of individuals with formerly fatal genetic defects. Therefore, in modern societies, the frequencies of genes for various formerly serious congenital abnormalities or for genetically influenced diseases will probably increase, though slowly.

Changes in social conditions or specific social trends may affect the distribution of genes by selective migration between and within larger populations. Large-scale immigration or transfer of population often will change gene frequencies in the areas of immigration and may do so also in the areas of emigration provided that the emigrating part of the population is genetically different from those who remain. There is little documented evidence for such selective emigration, but, as Stern pointed out, lack of evidence does by no means signify absence of the phenomenon; it is much more likely that emigration has some genetically selective aspects than that it lacks them. Certainly one of the important tasks for the future should be to determine quantitatively the degree of influence which emigration and immigration have on the distribution of genes.

Internal migration, from rural to urban areas and in the opposite direction, and social mobility which attracts and discharges specific individuals to and from various occupations and socio-economic layers are liable to form sieves through which some genetic types can pass and others are retained.

While changes in public health measures and medicine may lead to true changes in the frequencies of genes, the various types of migration at first simply change the distributions of genes. Since the patterns of reproduction of different populations, urban and rural sections, different occupational groups and different socio-economic layers vary, changes in the distribution of genes between different groups must result in changes in over-all gene frequencies. Koya raised the question as to possible selective effects of the present high rate of abortion in Japan.

Genic reproductive fitness is a relative property. In single dose many genes have no obvious effect on the fertility of their carriers while in double dose they may reduce it to zero. Moreover, the rest of the many thousand genes which make up the genetic material of a human is important. In different "genetic backgrounds" a given gene may have very different fitness, and so manifold are the interrelations of genes in development, growth and reproductive fitness that the opposition "single gene versus genetic background" may lose all precision. The human traits are the result of polygenic systems whose components often are not separable.

Even when a meaningful definition can be given to the term reproductive fitness for a given gene, the frequencies and distributions of the gene in future generations cannot be predicted. Fitness depends upon the specific environment. Changes in the external milieu can increase the fitness of poorly fit genotypes, making them more

likely to survive and changing the fitness of better ones. Obvious examples of improved fitness pertain to sugar diabetes with the discovery of insulin or to eye defects with the invention of optical and surgical remedies. Important examples of changed fitness in a changed social environment have been adduced by Sjögren: the genetic basis for dyslexia (writing and reading difficulties) may have become subject to negative selection in literate societies while it may be neutral in illiterate ones. Similarly, certain high-grade mental deficiencies imply a rather moderate social handicap in non-industrialized communities but may become seriously disadvantageous in industrial systems. In Sjögren's striking phraseology "these forms of oligophrenia—without any genetic change or any change in the clinical picture having taken place—have acquired an increased malignancy." Considering differential fertility, this social malignancy may actually imply increased reproductive fitness. The meeting was not charged with value judgments and hence did not express opinions on whether a relative increase in such genotypes was desirable.

Selection may be directed against or in favor of heterozygotes. Dependent on how widespread positive selection is as compared to negative selection for heterozygotes, the genetic consequences of intercrossing of formerly separated human groups will be very different.

Nachtsheim presented rates of mutation for various pathological genes, ranging from 1×10^{-2} to 1.2×10^{-5}. It is likely that such rates of spontaneous mutation will remain more constant than intensities of selection. This will lead to slow changes in the frequencies and distributions of genes. In particular, there will be an increase in the proportion of those genes involved in diseases and abnormalities whose origin by mutation is not sufficiently counterbalanced by selection. This increase in pathological genes is particularly likely because of the long-range effects of reduced selection due to the saving of lives by therapeutic measures. Artificial increases of potentially unfavorable genes are also bound to occur because of the widespread use of mutagenic radiations of medicine and industry, not to speak of war.

Formerly, geographically or sociologically separated populations and subpopulations — so-called isolates — reproduced within themselves. They became genetically different from one another as the result of selective forces or of chance.

The break-up of isolates due to better transportation and other factors leads to a scattering of clusters of like genes over the population at large. One consequence of this is, at least temporarily, a decrease of homozygotes, thus reducing the number of individuals homozygous for deleterious recessive genes. This reduction, however, will not take place with traits which depend on recessives with relatively high frequency or on dominant genes.

The reduction in deleterious homozygotes will often shield from negative selection those genes which become carried increasingly in healthy heterozygotes. Very slowly, mutation will fill up the new population with the shielded gene until the proportion of homozygotes rises to the former level.

The loss of adaptive gene combinations by isolate breaking is difficult to evaluate. The future seems likely to bring a large scale redistribution of genes by the interbreeding of diverse populations. Our present knowledge is too incomplete to foretell the consequences of such intermingling. Many geneticists feel that the result will not be harmful. Others are hesitant to adopt such a view so long as it has no basis in objective studies. The increased independence of modern man from formerly restrictive environmental agents may often —but perhaps not always—mean that no loss of adaptiveness is involved.

The elimination of morbid mutations can be achieved more efficiently by birth selection than by death selection; and this does not necessarily imply an authoritarian

abridgement of the freedom of action of the individual. Present frequencies and distribution of human genes are the result partly of processes beyond the control of man, and partly of man's voluntary actions and inactions. In an increasing manner, future frequencies and distributions will be predictable on the basis of human activities. This will mean increased responsibility since whatever we do or omit doing has its definite inescapable consequences.

The Need For Objective Data and Critical Research

There was general agreement that the only way to follow and control and study the whole body of pathologic genes in a population, "our load of mutations," is through a permanent systematic and thorough medico-genetic registration, a recording or reporting system, comprising all the patients in the population who are afflicted with a serious hereditary condition and also their families. This view was stressed by Leon, Evang, Kemp and others.

Such an epidemiological, genetic-hygienic control can be established in districts, regions or countries where the civilization has developed to a certain stage. The public health system and social care must be well-organized. Hospitals and other institutions for diseased and defective as well as the public care system must have attained a certain standard.

By means of such a genetic-hygienic registration we can follow the hereditary diseases in a population. We can check on their behavior. We can ascertain whether they decrease or increase in frequency and form an estimate as to whether the genetic-hygienic measures are carried through in the right way. Ultimately we can limit their prevalence.

Thorough instruction in human genetics, especially genetic pathology, ought to be included in the cirriculum of medical schools.

There is need to break down the barriers between disciplines, as pointed out by Lacroix, Aubenque and Kirk. International action is needed to standardize or at least to clarify definitions and terms. "Psychosis" for example is, as we know, not only a medical but certainly also a social diagnosis. Confusion will undoubtely arise unless great care is taken in defining terms.

In regard to nearly every aspect of human genetics, the nature-nurture problems are with us. Their solution, specific for each trait, is of prime importance to reaching conclusions on the distribution of genes in the population. Studies of maternal age and birth order throw light on these problems, as shown by McKeown. The review of twin studies by Gedda emphasizes the importance of twins as most valuable material for the evaluation of the hereditary and environmental components of an unlimited range of traits. There should be a world-wide search for the largely untapped reservoirs of identical twins reared apart. More work should be done in co-twin control research and with the "twin-family method," as well as in studies of foster children and orphans.

These conclusions on the importance of twin studies in the field of psychogenetics and psychosomatics meet with the expectation of the animal psychologists, as reported by Scott and Fuller, that the development of methods of measuring basic emotional and physiological differences at the earliest possible point in development is basic to an understanding of present and future distributions of human genes.

If, as seems likely, knowledge of human genetics increases as rapidly in the next ten years as in the years since the war, studies in the genetic qualities of populations can be expected to play a constantly increasing role in advancing human welfare. We may close with the words of Sauvy: "The sciences of demography and human genetics share a common ground. Their union can be exceedingly fruitful for the future of the human race."

BOOK REVIEWS

A Methodological, Psychiatric and Statistical Study of a Large Swedish Rural Population: Acta Psychiatric et Neurologica Scandinavica Supplementum 89, Tage Larsson and Torsten Sjögren; Donald Burton, Translator; Ejnar Munksgarrd, Copenhagen, 1954, 250 pp.

In 1948, Professor Sjögren reported in the same monograph series the results of an investigation of the prevalence and genetic linkage of psychiatric disorders and mental deficiency in the population of a small island off the west coast of Sweden. The present monograph presents partial data on a larger population resident on a second nearby island in addition to that already described. It considers methodological issues and presents basic statistics on the demography of the area, the prevalence of psychosis and severe mental defect, the mortality experience of psychotics and mental defectives and the overall morbidity risks for psychiatric disorders in this population. A subsequent volume will present the data bearing on genetic and clinical aspects of the research.

The aim of the larger study has been "to make a genetic and statistical analysis of psychoses and low-grade oligophrenia based on a thorough inventory of cases over a relatively long period in a geographically limited area and on a genealogical survey of the cases concerned and their families." The study area, designated as AB:bo, comprises thirteen parishes. The population of these parishes declined from about 30,000 in the 1900's to just under 22,000 in 1945, largely as a result of outward migration to neighboring districts and to a relatively nearby city. There are no towns of any size within AB:bo, indeed, only about a third of the population lived in agglomerations having as many as 200 persons. Roughly two-thirds of the population were engaged in agriculture, fishing and navigation.

As in previous studies conducted by European scholars in this field, the research began with designation of a group of probands, taken in this case as all persons with psychosis, severe psychopathy, and low-grade mental defect born in the investigation area or resident there who were registered as possessing such a disease or defect sometime during the period 1900 through 1945. There were three sources of registration: the records of the vicars in the parishes, the mental hospitals serving this area and the neighboring districts to which migrants from this area have gone, and the welfare organization which serves the larger county. A total of 745 psychotic and psychopathological probands was accumulated. Roughly five-sixths of the psychotics had been hospitalized, so that the chief source of data on these cases consisted of hospital records. Most of the remaining cases of psychiatric disorder were secured through the parish registers. By Swedish law, the vicar of each parish maintains certain population registers within which are to be designated all persons in the parish suffering from mental disease or mental defect. In recent years, however, these registers have apparently not been well maintained; nearly one-third of the hospitalized cases were not noted in the parish registers. In the case of the mentally defective however, the parish registers accounted for more than 90 per cent of the total cases designated as probands.

Despite the incompleteness of the parish registers, they served as a very useful basis for estimating the duration of time from onset of psychosis to first hospitalization. For all major diagnoses except senile psychosis, the median period between onset and hospitalization was over one year. For

schizophrenic and manic-depressive psychosis between one-fourth and one-third of the probands had been registered in the parish as mentally ill more than five years before their hospitalization. These data are particularly valuable for attempting to estimate the excess mortality of the mentally ill, in the period prior to their hospitalization. The index used in describing the mortality experience of psychotics is the percentage of normal life expectation, using appropriate life tables, calculated from the time of onset of the disease. Schizophrenics and low-grade mental defectives were both found to have about 70 per cent of the normal life expectation.

The total morbidity risks for schizophrenia and other psychoses, using the method of Weinberg for estimation of population exposed to risk, run substantially higher than those found in other population studies. Indeed, Kallmann has used an estimate of 1 per cent based on Sjögren's previous work as the maximum expectancy, but the present study raises that figure to 1.6 per cent. The increase is largely the result of correcting for excess mortality and distributing cases of undiagnosed psychosis as though they had the same relative frequencies as diagnosed cases. The aggregate morbidity risk for all forms of psychosis was found to be 4.7 per cent for men and 5.7 per cent for women. The rates for mental defect—representing roughly that portion of the population with I.Q. under 55—were found to be 1 per cent for men and .75 per cent for women.

One is impressed with the great care which has gone into the analysis of the materials secured in this study. The work is typical of European studies which seek precision of computation while giving relatively little consideration to alternative methods of case-finding which might markedly change the rates obtained. One may say that, on the whole, German and Scandinavian scholars have assumed the genetic factor to be all important and have been almost completely oblivious of social and cultural factors which may influence both the frequency of mental illness and the frequency of its recognition. American students have been much more concerned with the fact that designation of a person as mentally ill is in the last analysis a social labeling and not merely a biological fact; indeed, they have tended to ignore the heredity factor in favor of social and cultural characteristics of the populations studied.

This work of Larsson and Sjögren should certainly be carefully studied by all scholars interested in the prevalence and incidence of mental illness, regardless of their theoretical persuasion. Any study of this kind will result in frustrations when one attempts comparisons with other populations, especially with studies done by scholars having a different orientation and approach. In the long run, however, comparability will be achieved only as workers with different persuasions show sufficient respect for alternative approaches so that they seek to encompass the problem area and not merely to demonstrate the importance of their own formulations.

One hopes that in the promised second volume there will be a more adequate indication of the techniques of field investigation, a description of the process whereby mentally ill persons come to be listed in the parish registers, and more complete specification of the diagnostic criteria used for classifying cases not diagnosed in a mental hospital. One related critical note must be added: In studies of this kind a translator must have skill not only in two languages involved but also in the relevant conceptual usage by scholars in both languages. The present monograph often requires several readings and consultation of other sources in order to understand what is being expounded.

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GENETICS, BIOLOGICAL INDIVIDUALITY AND CANCER: Clarence C. Little, Stanford University Press, Stanford, California, 1954, ix, 115 pp., 27 figures, $2.50.

This little paper-bound volume contains the Lane Medical Lectures delivered at Stanford University in February, 1954. The book sets forth what may be called "The Unbalance Theory of Cancer." The author contends that growth and multiplication are primary tendencies of living cells, and that the normal failure of cells to multiply exponentially in adult mammals is the result of a delicate and rather unstable equilibrium between the vitality of the cell, on one hand, and the control exercised by the organism on the other. It therefore seems proper to ascribe cancer to release of the cell's growth potential, rather than to stimulation of growth as some theories do.

Controlled cellular growth, like other balanced biological states, appears to be determined largely by genetic factors, and genetic unbalance, for example, after hybridization, frequently results in uncontrolled or cancerous growth of cells. However, many other mechanisms may also disturb the balance of the cell and are potential causes of cancer. The directions in which this discussion leads are best seen in the chapter headings: Latent Growth Potential, Biological Individuality, Hybridization and Unbalance, Hormones and Unbalance, Intracellular Unbalance, and Unbalance by Viroids.

The effect of Dr. Little's Unbalance Theory is to discourage the search for a singe cause or a single cure for cancer, for a great variety of agents may cause cancer in a great many ways. The book helps to explain what has long been clear to cancer researchers, that almost anything we learn about cell growth, cell physiology, and even about viruses, may advance our understanding of cancer.

Although Dr. Little bases the discussion on his own experience with mice, he brings in countless other illustrations to support his generalizations. The multiplication of examples is perhaps the only feature that prevents the book from being enjoyable reading for the non-specialist. The same feature, however, renders these lectures a permanent and perhaps a classical contribution to cancer literature.

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PERIODICAL ABSTRACTS

*GENETICS**

Huntington's chorea in Northamptonshire. M. J. Pleydell. *British Medical Journal* 2 (1954), pp. 1121–1128.

The author, a British health officer, explains that this hereditary disease is a public health problem of serious magnitude and advocates appropriate combative measures. The disease is first detected at an average age of 35. It results in involuntary movements and mental deterioration which progress to a fatal termination after an average interval of 14 years. In the early stages of the disease there is sometimes a heightened sexual interest, which helps to account for the apparently high fertility in affected families. The condition is inherited as a dominant, and affected persons usually give a history of the disease in a parent and a grandparent, as well as in aunts, uncles and siblings.

A survey of Northamptonshire county disclosed 13 cases in six families, or a frequency of five patients per 100,000 population. If this figure is representative, there may be 2000 af-

*Papers abstracted in this column are not necessarily offered as the best or the most important papers appearing on human genetics. They are selected because they appear to be relevant to eugenics and comprehensible to non-geneticists. Generally they are papers which present definite conclusions or which illustrate important trends in genetic research.

fected persons in England and Wales alone, most of them undiagnosed. Families generally fail to understand the hereditary nature of the disease, but live in dread of it. Since it is inherited as a dominant trait, each person with an affected parent could be told at the usual marriage age that he has a 50 per cent chance of escaping the disease, but a 25 per cent chance of transmitting it to any one of his own children.

Five approaches are recommended as public health policy: (1) Reporting of all diagnosed cases so that the public health authorities can investigate close relatives, as is done now in cases of tuberculosis. (2) The counseling of all persons with affected parents against childbearing or against marriage. (3) Termination of pregnancies when either parent has the disease or is likely to have it. (4) Maintenance of friendly contact with, and supervision of, every affected family. (5) Prompt institutionalization of cases that have become difficult to manage at home.

The assimilation of the descendants of immigrants. Corrado Gini. *Acta Geneticae Medicae et Gemellologiae* **3** (1954), pp. 270-275.

Immigrants that settled in South Italy about five centuries ago have been completely assimilated into the Italian population insofar as this can be assessed anthropologically. Not only do they resemble the surrounding Italians when taken as a group, but those individuals with the smallest proportion of acknowledged Italian ancestry were found to have the same anthropometric traits, on the average, as those who claimed mainly Italian ancestry. This is especially striking in some Albanian settlements, which preserve their original language, costume, and culture but have lost the tall stature and round heads characteristic of Albania. Groups of North Italians that have settled in Sicily within the past two centuries retain both culture and physical features of North Italy, but they show a clear tendency toward increase of pigmentation with age and from one generation to the next. The author doubts that these changes can be entirely explained on the basis of intermarriage with Italians. He thinks the environment must have an influence in molding "racial" characteristics, either directly or by selection.

The significance of this research would be greatly enhanced by the addition of blood-group studies. In the case of racial stocks that have lived in Italy for 500 years, it would seem difficult to establish the proportion of Italian admixture merely by interrogating the subjects.

"Studies on the human sex ratio." 4. Evidence of genetic variation of the primary sex ratio in man. Marianne E. Bernstein. *Journal of Heredity* **45** (1954), pp. 59–64.

In a previous study the author classified men in "Who's Who in America" according to masculine, feminine and neutral occupations, and found 55.6 per cent males among the offspring of men in masculine occupations and 45.5 per cent among those of men in feminine occupations.

In the present study, data taken mainly from "American Women" revealed a comparable effect of mother's occupation. Occupations of parents appear to have an additive effect, and when both are in masculine occupations the proportion of male offspring is 12 percentage points higher than when both are in feminine occupations. The author believes that abortion rates are so low in the socio-economic group studied that the variation must represent variation in the sex ratio at conception. She outlines a novel hypothesis that would explain her findings.

Notes on sickle-cell polymorphism. A. C. Allison. *Annals of Human Genetics* (formerly, *Annals of Eugenics*) **19** (1954), pp. 39–51.

Sickle-cell anemia is a condition in which an abnormal form of hemoglobin results in distortion of the red blood corpuscles and in their destruction at a rate that leaves the person severely anemic. It is inherited as a recessive character but heterozygotes (healthy carriers) are easily recognized by the fact that their red blood cells are distorted into crescents when deprived of oxygen in the laboratory. The latter condition is known as the sickle-cell trait.

The sickle-cell trait is common in American Negroes, and still more common in certain African tribes and in other scattered tropical peoples. The extreme variability of tropical man with respect to this hereditary trait is difficult to explain in terms of ancestral origins alone. Furthermore, there is a constant and effective elimination of sickle-cell genes: persons having sickle-cell anemia, each carrying two of the genes, rarely survive to have children. The high incidence of the trait in certain populations might be explained by assuming that the loss of genes is made up by very frequent new mutations. An alternative explanation would be that the sickle-cell trait, in the healthy carriers, is somehow advantageous, and is favored by natural selection. Such an advantage appears, in fact, to exist in areas where malaria of the most severe type is very common. In such areas, children with the sickle-cell trait are apparently more resistant to malaria than children

with normal blood. Among those who survive to reproduce, therefore, the frequency of the sickle-cell trait is relatively high. This increase in the frequency of carriers of the gene in each generation is presumably just enough to compensate the loss of genes in those who die prematurely because of sickle cell anemia.

In populations like the American Negro that have been removed from exposure to malaria, the selective advantage of the sickle-cell trait disappears. The gene frequency is therefore expected to drop in each generation. Actually, the incidence of sickling observed in modern American Negroes is less than half the postulated frequency in their African ancestors. This is almost exactly what would be predicted mathematically on the hypothesis that malaria maintains the gene at a high frequency in Africa.

The sickle-cell trait is an apparent instance of "balanced polymorphism," as in the Rh factor (see EUGENICS QUARTERLY 1, 1954, 2 pp. 59–60). By analogy with fruit flies, it now appears likely that this situation exists with respect to a great many human hereditary traits, and that natural selection would not produce a uniform human type even after an infinite number of generations.

An estimate of the frequency of phenylketonuria in South Sweden. Carl A. Larson. *Folia Hereditaria et Pathologica* 4 (1954) pp. 40-46.

Twenty-eight cases of this recessive hereditary disease were found among 4,825 institutionalized mental defectives drawn from a population of 3.4 million. To this figure must be added an estimate of non-institutionalized cases, mainly morons. Although the disease is relatively infrequent among morons, these high-grade defectives are so numerous in the general population that they may contribute a major proportion of all phenylketonuria. A few cases even occur in the borderline and normal groups.

The author estimates that in every 100,000 of the total population, 1.1 are seriously defective and 2.4 are morons as a result of phenylketonuria, a total incidence of 3.5 per 100,000. An independent estimate based upon the frequency of cousin marriages among parents of the patients suggested a frequency of 2.5 per 100,000. Even at this lower figure, one person in every 100 would be a carrier of the gene for phenylketonuria. Estimates obtained in America and Great Britain are in rather close agreement with this figure.

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National Institute of Mental Health

POPULATION

Trends in occupational origins of business leaders, Stuart Adam, *American Sociological Review*. 19 (1954) pp. 541–548.

Data on this subject were secured from "a combination of mailed questionnaires and follow-up interviews with selected non-respondents. The questionnaires were mailed to 510 'business owners or executives employing 100 or more persons' in two geographical regions—Worcester and Springfield, Massachusetts; and Columbus and Toledo, Ohio" (p. 542).

There were 178 mail returns and 42 interviews from the 510 possible informants. The findings suggested no regional difference and no clear-cut time trend in the occupational origins (paternal occupations) of the business leaders considered. There was some evidence of a curvilinear relation of occuational origin to size of business enterprise. The authors state that since the respondents considered were born during 1900–1910 the results may have been complicated by the inclusion of the economic depression in the time-period considered.

Social mobility and mental illness, A. B. Hollingshead, R. Ellis, and E. Kirby. *American Sociological Review*, 19 (1954), pp. 577-584.

To test the proposition that vertical mobility is associated with the development of phychiatric disorders, the authors undertook a study of samples of "the psychiatric population of the New Haven community." The sample was designed as follows: "sub-samples of psychoneurotic and schizophrenic patients in Classes III [proprietors of small businesses, white-collar workers, and skilled workers of high school status] and V [unskilled and semi-skilled workers of elementary school status and residents of slum areas.] Control groups of 30 non-patients from Classes III and IV were drawn for purposes of comparison.

The study is concerned with two types of mobility factors; (a) achieved social mobility and (b) discrepancy between an individual's achievements and his aspirations.

The samples studied are too small to yield more than suggestive findings. The authors state: "Vertical mobility has been shown to be a factor of significance in both schizophrenia and psychoneurosis, in the representative samples of two classes of the New Haven population. . . . It seems clear . . . that relations between status striving, anxiety, and mental health, deserve further intensive investigation."

CLYDE V. KISER
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